RECEIVED

SEQUENCE LISTING

<110> Cortes, J
 Fromentin, C
 Gaisser, S
 Leadlay, P
 Mendez, C
 Michel, J-M
 Raynal, M-C
 Salah-Bey, K
 Salas, J



<120> BIOSYNTHESIS GENES & TRANSFER OF 6-DESOXYHEXOSES IN SACCHAROPOLYSPORA ERYTHRAEA AND IN STREPTOMYCES ANTIBIOTICUS AND THEIR USE

<130> 146.1335

<140> 09/463705 <141> 2000-02-23

<150> PCT/FR98/01593

<151> 1998-07-21

<150> 98/07411

<151> 1988-06-12

<150> 97/09458

<151> 1997-07-25

<160> 61

<170> PatentIn Ver. 2.1

<210> 1

<211> 3439

<212> DNA

<213> Saccharopolyspora erythraea

<220>

<221> CDS

<222> Complement((48)..(1046))

<223> /function= "involved in the biosynthesis of mycarose" /qene= "eryBII"

<220>

<221> CDS

<222> Complement((2322)..(3404))

<223> /function= "involved in the biosynthesis of desosamine" /gene= "eryCII"

<400> 1

getteaeget caccageegt atcetttete ggtteetett gtgeteaetg caaccagget 60

teeggegeeg egeegeegga ggecaeegeg gggaagatet egteeagtte ggaeagegee 120

tgctcgtcca gggtcatcgc ggacgccttc agcgcggagt cgagctgctc gggggttcgc 180

gggccgatga cggcgccggc gatgccgggc cgggacagca cccatgcgag ccccacctcg geogggtett egeogaggtt geggeagaac ttetegtagg cetegatege egggegeagg 300 gaeggeaaca geacetgege aeggeeetge geegaettea eegeggtgee egeggeeage 360 420 ttctccageg ctccgctgag caggccgccg tgcagcggcg accaggcgaa gacgccgagc 480 cegtaggeet gegeggeggg cageacetee ageteggegt geeggacege caggttgtae aggcactggt gggagaccat gcccagggag tggcggcggg cggcgttctc ctgcgcggcg 540 gegatgtgcc agcccgcgaa gttcgacgag ccgacgtagg agaccttgcc gctggcgacg 600 660 aggetgteca tggeetgeea caeetegtee caeggegegg aceggtegat gtggtgeate 720 tggtagacgt cgatgtggtc gacgcccagc ctgcgcagcg atccctcgca ggaggcgatg atgtgccgcg ccgacagccc gctgtcgttg acgcgctcgc tcatctcgcc gccgaccttg 780 gtcgccagca cggtgtcctc gcgccgtccg ccgccctggg ccagccacct gcccaccagc 840 900 tecteggtgt ggeeettgta gageegeeag eegtaeatgt eggeggtgte gaggeagttg atgccgcggt cccgggcgtg gtccatcagg cgcagcgcgt cgtcgtcctc gacgcgtccg 960 1020 ctgaagttca ccgtgccgag ccagagcctg ctggtgagca gcgcggaacg cccgagccgc acgtgcgtcg cggcgtcggt ggtcatcgtg gttctctcct tcctgcggcc agttcctcgc 1080 agatgeegae gaceteggee ggtgaegget eegegageat gtegtegege ateegegeeg 1140 cgccggcgcg gtgggccggg tcgtcgagga cccgcttcac cgactcccgg agctggtcgg 1200 gggtcagctc gggcacgggc agcgcgatcc ccgccccgaa ttcctgcgtg cgctgcgcg 1260 gcacgccggt gtcccagccg tcgggcagga tcacctgcgg cacgccgtgg atcgccgcgg 1320 tgtgccaget ecegggteeg eegtggtgea eegtegeege geaggtegge ageagegegt 1380 gcatcgggac gaagccgacc gtgcggacgt tgtccgggat gttcgcgacg ccttctagct 1440 gctgcgcgtc gaaggtcgcg atgatctcgg cgtcgacgtc gccgacggca cccagcagct 1500 cctcgatgga gacctgcccg atgctgttct cgcggctgga gatcccgagc gtgaggcaca 1560 egeggeggeg etegggeteg tegtgeagee atteeggeae eaeggaegge eegttgtagt 1620 cgacgtageg catecegaeg gtetteagge eggtgtegag cetgategeg geeggggegg 1680 1740 ccagcgtcca ggtgagccac tcggcgagcg ggtcctcccg gtgctcctcc ggctggtcgg 1800 gcagcaggcc gaggaagttc tgccgcgccc gggtggtgat gtcgggtccc cacagcagcc 1860

gegegtgegg egtteeggte acegeegeeg egatgggege ggegaaggtg ageggeteee agatgaccag gtcgggccgc cacttccggc agaacgagac catgccttcg atgagcgtgt 1980 eegggeteat eagggegtag aaggtegggg tgageaeggt etgeatgeee ageaggtget 2040 cccaggtcaa ggtggcgggg tcccgctcgc tgaagtccag gctccggacg tagtcgatga 2100 tgtcgtggcc cgcgtgggtc atgaagtcca cgaggtcgac gtcggtgccg accgggacgg 2160 eggteageee ggeegeggtg atgteetegg tgagegeegg ggaegegaee aegeggaeet 2220 2280 cgtgccccgc cgcgcggaac gcccatgcga gggggacgag gccgaagagg tggctcttgc tggccatgga ggagaagacg acgcgcatcg cggttacctc agagctcgac ggggcagcgg 2340 ttggttcccc gcaggacggg tgatcggcgg cgccggacga ccgggccgct gggcgtgagt 2400 cegggcageg cettggcege ggcccgcagt geggeggtgg cgagcgcggt gaccagetee 2460 tecageetge eggggtggee gegatgtgee gacagegege ggteggegte ggggeggtee 2520 2580 acgtcgaggc ggtcgggctc ggcgaagacc tccgggtcgc ggttggccgc cgcgacgacg accacgacet cetegeette geogateaeg tgetegeega geogeaeete tgeggtggee 2640 gtgcgccgct ccaggtgcaa tgccgggtgc aggcgcagca cctcggcgac ggttcgctgc 2700 2760 gcggcggcgg ggtcgtcggc gatccgttcg gccagccccg gttcggccga gacggccagg 2820 accgcgtcga ccacggtgtt cgcggtcatc tcggccccgg cgaacagggc gcgcagtgcg gggtcggcgg gcagtgccgc gaccgctgct tcggtcaccg cgagctgctg cgggctgagc 2880 2940 tgggcgtcca ggctgacgcg ggcgtcccac gcggcgccgc gcagcactcc ggctgcgccg 3000 agcacggcgg tcatgccctg caccggtacc tgccaggcga agtcgccgac caggtccagc egegegeeeg egeeggggag eagaceggeg aageteteeg eeagtteeee gaegtegggg 3060 acctegeett ceeaggaege ggegtgeaeg teeeggaaeg getgggeeea eteggegggt 3120 ggegegeceg eggeeegeat ceatteeggt gtgegteegg tggegegggt gaacgegggg 3180 tegtegagea cetgeeggge ggtggegtgg teggeeacea cecaegtete ggtgeggetg 3240 cgccgcacac cggactcgcg catcgagcgg taccggcgct gcgggtcgtc gtcgtgtccg 3300 cacagcagca tegggtaagg gtegeegttg etgeegtaac cecagtgeag geegeggate 3360 atctggaget geetgeecag eeeggegega teggtegtgg teatgaatte eeteegeeca 3420 gccaggcgtc gatgtgccg 3439

<210> 2 <211> 333 <212> PRT

<213> Saccharopolyspora erythraea

<400> 2

Met Thr Thr Asp Ala Ala Thr His Val Arg Leu Gly Arg Ser Ala Leu

1 5 10 15

Leu Thr Ser Arg Leu Trp Leu Gly Thr Val Asn Phe Ser Gly Arg Val
20 25 30

Glu Asp Asp Asp Ala Leu Arg Leu Met Asp His Ala Arg Asp Arg Gly
35 40 45

Ile Asn Cys Leu Asp Thr Ala Asp Met Tyr Gly Trp Arg Leu Tyr Lys
50 55 60

Gly His Thr Glu Glu Leu Val Gly Arg Trp Leu Ala Gln Gly Gly Gly 65 70 75 80

Arg Arg Glu Asp Thr Val Leu Ala Thr Lys Val Gly Glu Met Ser 85 90 95

Glu Arg Val Asn Asp Ser Gly Leu Ser Ala Arg His Ile Ile Ala Ser 100 105 110

Cys Glu Gly Ser Leu Arg Arg Leu Gly Val Asp His Ile Asp Val Tyr 115 120 125

Gln Met His His Ile Asp Arg Ser Ala Pro Trp Asp Glu Val Trp Gln 130 135 140

Ala Met Asp Ser Leu Val Ala Ser Gly Lys Val Ser Tyr Val Gly Ser 145 150 155 160

Ser Asn Phe Ala Gly Trp His Ile Ala Ala Ala Gln Glu Asn Ala Ala 165 170 175

Arg Arg His Ser Leu Gly Met Val Ser His Gln Cys Leu Tyr Asn Leu 180 185 190

Ala Val Arg His Ala Glu Leu Glu Val Leu Pro Ala Ala Gln Ala Tyr 195 200 205

Gly Leu Gly Val Phe Ala Trp Ser Pro Leu His Gly Gly Leu Leu Ser 210 215 220

Gly Ala Leu Glu Lys Leu Ala Ala Gly Thr Ala Val Lys Ser Ala Gln 225 230 235 240

Gly Arg Ala Gln Val Leu Leu Pro Ser Leu Arg Pro Ala Ile Glu Ala 245 250 255

Tyr Glu Lys Phe Cys Arg Asn Leu Gly Glu Asp Pro Ala Glu Val Gly

Leu Ala Trp Val Leu Ser Arg Pro Gly Ile Ala Gly Ala Val Ile Gly 275 280 285

Pro Arg Thr Pro Glu Gln Leu Asp Ser Ala Leu Lys Ala Ser Ala Met 290 295 300

Thr Leu Asp Glu Gln Ala Leu Ser Glu Leu Asp Glu Ile Phe Pro Ala 305 310 315 320

Val Ala Ser Gly Gly Ala Ala Pro Glu Ala Trp Leu Gln 325 330

<210> 3

<211> 361

<212> PRT

<213> Saccharopolyspora erythraea

<400> 3

Met Thr Thr Asp Arg Ala Gly Leu Gly Arg Gln Leu Gln Met Ile 1 5 10 15

Arg Gly Leu His Trp Gly Tyr Gly Ser Asn Gly Asp Pro Tyr Pro Met
20 25 30

Leu Leu Cys Gly His Asp Asp Pro Gln Arg Arg Tyr Arg Ser Met 35 40 45

Arg Glu Ser Gly Val Arg Arg Ser Arg Thr Glu Thr Trp Val Val Ala 50 55 60

Asp His Ala Thr Ala Arg Gln Val Leu Asp Asp Pro Ala Phe Thr Arg 65 70 75 80

Ala Thr Gly Arg Thr Pro Glu Trp Met Arg Ala Ala Gly Ala Pro Pro 85 90 95

Ala Glu Trp Ala Gln Pro Phe Arg Asp Val His Ala Ala Ser Trp Glu 100 105 110

Gly Glu Val Pro Asp Val Gly Glu Leu Ala Glu Ser Phe Ala Gly Leu 115 120 125

Leu Pro Gly Ala Gly Ala Arg Leu Asp Leu Val Gly Asp Phe Ala Trp 130 135 140

Gln Val Pro Val Gln Gly Met Thr Ala Val Leu Gly Ala Ala Gly Val 145 150 155 160

Leu Arg Gly Ala Ala Trp Asp Ala Arg Val Ser Leu Asp Ala Gln Leu 165 170 175

Ser Pro Gln Gln Leu Ala Val Thr Glu Ala Ala Val Ala Leu Pro 180 185 190

Ala Asp Pro Ala Leu Arg Ala Leu Phe Ala Gly Ala Glu Met Thr Ala 195 200 205

Asn Thr Val Val Asp Ala Val Leu Ala Val Ser Ala Glu Pro Gly Leu

- 5 -

210 215 220

Ala Glu Arg Ile Ala Asp Asp Pro Ala Ala Ala Gln Arg Thr Val Ala 225 230 235 240

Glu Val Leu Arg Leu His Pro Ala Leu His Leu Glu Arg Arg Thr Ala
245 250 255

Thr Ala Glu Val Arg Leu Gly Glu His Val Ile Gly Glu Glu Glu Glu 260 265 270

Val Val Val Val Ala Ala Ala Asn Arg Asp Pro Glu Val Phe Ala 275 280 285

Glu Pro Asp Arg Leu Asp Val Asp Arg Pro Asp Ala Asp Arg Ala Leu 290 295 300

Ser Ala His Arg Gly His Pro Gly Arg Leu Glu Glu Leu Val Thr Ala 305 310 315 320

Leu Ala Thr Ala Ala Leu Arg Ala Ala Lys Ala Leu Pro Gly Leu 325 330 335

Thr Pro Ser Gly Pro Val Val Arg Arg Arg Arg Ser Pro Val Leu Arg 340 345 350

Gly Thr Asn Arg Cys Pro Val Glu Leu 355 360

<210> 4

<211> 1266

<212> DNA

<213> Saccharopolyspora erythraea

<220>

<221> CDS

<222> complement (4)..(1266)

<223> /function= "involved in the biosynthesis of mycarose" /gene= "eryCIII" /note= "SEQ ID No 1 from 1046 to 2308"

<400> 4

 زيز

gatctcggcg	tcgacgtcgc	cgacggcacc	cagcagctcc	tcgatggaga	cctgcccgat	480
gctgttctcg	cggctggaga	tcccgagcgt	gaggcacacg	cggcggcgct	cgggctcgtc	540
gtgcagccat	tccggcacca	cggacggccc	gttgtagtcg	acgtagcgca	tcccgacggt	600
cttcaggccg	gtgtcgagcc	tgatcgcggc	cggggcgggg	tcgatcgtcc	actgcccgac	660
gaccacctcc	tcgtcgaagg	ccgggccgcc	gtacttctcc	agcgtccagg	tgagccactc	720
ggcgagcggg	tcctcccggt	gctcctccgg	ctggtcgggc	agcaggccga	ggaagttctg	780
ccgcgcccgg	gtggtgatgt	cgggtcccca	cagcagccgc	gcgtgcggcg	ttccggtcac	840
cgccgccgcg	atgggcgcgg	cgaaggtgag	cggctcccag	atgaccaggt	cgggccgcca	900
cttccggcag	aacgagacca	tgccttcgat	gagcgtgtcc	gggctcatca	gggcgtagaa	960
ggtcggggtg	agcacggtct	gcatgcccag	caggtgctcc	caggtcaagg	tggcggggtc	1020
ccgctcgctg	aagtccaggc	tccggacgta	gtcgatgatg	tcgtggcccg	cgtgggtcat	1080
gaagtccacg	aggtcgacgt	cggtgccgac	cgggacggcg	gtcagcccgg	ccgcggtgat	1140
gtcctcggtg	agcġccgggg	acgcgaccac	gcggacctcg	tgccccgccg	cgcggaacgc	1200
ccatgcgagg	gggacgaggc	cgaagaggtg	gctcttgctg	gccatggagg	agaagacgac	1260
gcgcat						1266

<210> 5

<211> 421

<212> PRT

<213> Saccharopolyspora erythraea

<400> 5

Met Arg Val Val Phe Ser Ser Met Ala Ser Lys Ser His Leu Phe Gly 1 5 10 15

Leu Val Pro Leu Ala Trp Ala Phe Arg Ala Ala Gly His Glu Val Arg
20 . 25 . 30

Val Val Ala Ser Pro Ala Leu Thr Glu Asp Ile Thr Ala Ala Gly Leu 35 40 45

Thr Ala Val Pro Val Gly Thr Asp Val Asp Leu Val Asp Phe Met Thr 50 55 60

His Ala Gly His Asp Ile Ile Asp Tyr Val Arg Ser Leu Asp Phe Ser 65 70 75 80

Glu Arg Asp Pro Ala Thr Leu Thr Trp Glu His Leu Leu Gly Met Gln 85 90 95

Thr Val Leu Thr Pro Thr Phe Tyr Ala Leu Met Ser Pro Asp Thr Leu

Ile Glu Gly Met Val Ser Phe Cys Arg Lys Trp Arg Pro Asp Leu Val 120 Ile Trp Glu Pro Leu Thr Phe Ala Ala Pro Ile Ala Ala Val Thr 135 Gly Thr Pro His Ala Arg Leu Leu Trp Gly Pro Asp Ile Thr Thr Arg 150 Ala Arg Gln Asn Phe Leu Gly Leu Leu Pro Asp Gln Pro Glu Glu His 170 Arg Glu Asp Pro Leu Ala Glu Trp Leu Thr Trp Thr Leu Glu Lys Tyr Gly Gly Pro Ala Phe Asp Glu Glu Val Val Gly Gln Trp Thr Ile Asp Pro Ala Pro Ala Ala Ile Arg Leu Asp Thr Gly Leu Lys Thr Val Gly Met Arg Tyr Val Asp Tyr Asn Gly Pro Ser Val Val Pro Glu Trp 235 Leu His Asp Glu Pro Glu Arg Arg Arg Val Cys Leu Thr Leu Gly Ile Ser Ser Arg Glu Asn Ser Ile Gly Gln Val Ser Ile Glu Glu Leu Leu 265 Gly Ala Val Gly Asp Val Asp Ala Glu Ile Ile Ala Thr Phe Asp Ala 280 Gln Gln Leu Glu Gly Val Ala Asn Ile Pro Asp Asn Val Arg Thr Val 295 Gly Phe Val Pro Met His Ala Leu Leu Pro Thr Cys Ala Ala Thr Val 305 310 His His Gly Gly Pro Gly Ser Trp His Thr Ala Ala Ile His Gly Val 330 Pro Gln Val Ile Leu Pro Asp Gly Trp Asp Thr Gly Val Arg Ala Gln Arg Thr Gln Glu Phe Gly Ala Gly Ile Ala Leu Pro Val Pro Glu Leu Thr Pro Asp Gln Leu Arg Glu Ser Val Lys Arg Val Leu Asp Asp Pro Ala His Arg Ala Gly Ala Ala Arg Met Arg Asp Asp Met Leu Ala Glu

Pro Ser Pro Ala Glu Val Val Gly Ile Cys Glu Glu Leu Ala Ala Gly

415

Arg Arg Glu Pro Arg 420

```
<210> 6
<211> 8160
<212> DNA
<213> Saccharopolyspora erythraea
<220>
<221> CDS
<222> (242)..(1207)
<223> /function= "involved in the biosynthesis of
      mycarose" /gene= "eryBIV" /transl_except= (pos:
      242 .. 244, aa; Met)
<220>
<221> CDS
<222> (1210)..(2454)
<223> /function= "involved in the biosynthesis of
      mycarose" /gene= "eryBV" /transl_except= (pos:
      1210 .. 1212, aa: Met)
<220>
<221> CDS
<222> (2510)..(3220)
<223> /function= "involved in the biosynthesis of
      desosamine" /gene= "eryCVI"
<220>
<221> CDS
<222> (3308)..(4837)
<223> /function= "involved in the biosynthesis of
      mycarose" /gene= "eryBVI" /transl_except= (pos:
      3308...3310, aa: Met)
<220>
<221> CDS
<222> (6080)..(7546)
<223> /function= "involved in the biosynthesis of
      desosamine" /gene= "eryCV"
<220>
<221> CDS
<222> (7578)..(8156)
<223> /function= "involved in the biosynthesis of
      mycarose" /gene= "eryBVII" /transl except=
      (pos:7578 .. 7580, aa: Met)
<220>
<221> mat_peptide
<222> (242)
<400> 6
```

- 9 -

tttgacaggt ccgccacgcg tccccctact cgacgaccac gcaatgggcg aacaatatag 60

gaag	gato	caa g	gaggt	tgad	ca to	gcct	cgto	gag	gccaa	acga	acct	gtga	aac a	atcto	gcatgt	120
tgad	caaga	atc a	aacgg	gegge	ct ac	ctac	ctgtg	g gto	ggcco	cagt	gaco	ggtt	gc o	gcac	atcgc	180
gcts	3 3 33	aga t	tctt	tgaa	at tt	cgcc	cgta	a gca	accga	acct	ggaa	agco	gag o	caaat	gctcc	240
	_			_	-			_	g G		-			eu Le	g ggc u Gly	
					Gly ggg											337
					gcg Ala										ccg Pro	385
					gtc Val											433
					gcg Ala 70											481
					ggc Gly											529
					gtc Val											577
					cgc Arg											625
_		_	_	_	gcg Ala		_	_		_	_				-	673
					gag Glu 150											721
					atc Ile											769
					atg Met											817
_	_		_		gag	_			_			_				865

195 200 205

cgc cgc gac c Arg Arg Asp I 210	Leu Leu His				_
gcg ctg gag o Ala Leu Glu F 225					
gcc gac cga t Ala Asp Arg S					
agc gtc gcc o Ser Val Ala <i>I</i>					
ccc gcg ccc g Pro Ala Pro (275			_		
gac tcc acc of Asp Ser Thr (Glu Phe Arg				
ctc acc gac of Leu Thr Asp (305					
gag cac ta gt Glu His Me				cac cgc acg o His Arg Thr H	
	et Arg Val L 325 ctg gtc ccg	eu Leu Thr S	Ger Phe Ala I 330 gcg ctg cgc	His Arg Thr H	His 335 cac 1296
ttc cag gga c Phe Gln Gly I gac gtg cgc g Asp Val Arg V	et Arg Val L 325 ctg gtc ccg Leu Val Pro 340 gtg gcc gcc	eu Leu Thr S ctg gcg tgg Leu Ala Trp cag ccc gcg	Ger Phe Ala I 330 gcg ctg cgc Ala Leu Arg 345 ctc acc gac	acc gcg ggt Thr Ala Gly 350 gcg gtc atc	His 335 cac 1296 His ggc 1344
ttc cag gga c Phe Gln Gly I gac gtg cgc g Asp Val Arg V	et Arg Val L 325 ctg gtc ccg Leu Val Pro 340 gtg gcc gcc Val Ala Ala 355 acc gcg gta	ctg gcg tgg Leu Ala Trp cag ccc gcg Gln Pro Ala 360 ccc gtc ggc	Ger Phe Ala I 330 gcg ctg cgc Ala Leu Arg 345 ctc acc gac Leu Thr Asp	acc gcg ggt Thr Ala Gly 350 gcg gtc atc Ala Val Ile 365 cgg ctg ttc	His 335 cac 1296 His ggc 1344 Gly gac 1392
gac gtg cgc gAsp Val Arg Val Ala Gly Leu S	et Arg Val L 325 ctg gtc ccg Leu Val Pro 340 gtg gcc gcc Val Ala Ala 355 acc gcg gta Thr Ala Val gaa gtc gcc Glu Val Ala	ctg gcg tgg Leu Ala Trp cag ccc gcg Gln Pro Ala 360 ccc gtc ggc Pro Val Gly 375 gct cag gtg	Ger Phe Ala I 330 gcg ctg cgc Ala Leu Arg 345 ctc acc gac Leu Thr Asp tcc gac cac Ser Asp His cac cgc tac	acc gcg ggt Thr Ala Gly 350 gcg gtc atc Ala Val Ile 365 cgg ctg ttc Arg Leu Phe 380 tcc ttc tac	His 335 cac 1296 His ggc 1344 Gly gac 1392 Asp ctg 1440
gac gtg cgc gas gga gtg cgc ggt ctc a Ala Gly Leu 370 atc gtc ccg gile Val Pro G	et Arg Val L 325 ctg gtc ccg Leu Val Pro 340 gtg gcc gcc Val Ala Ala 355 acc gcg gta Thr Ala Val gaa gtc gcc Glu Val Ala cac cgc gag	ctg gcg tgg Leu Ala Trp cag ccc gcg Gln Pro Ala 360 ccc gtc ggc Pro Val Gly 375 gct cag gtg Ala Gln Val 390 cag gag ctg	Ger Phe Ala I 330 gcg ctg cgc Ala Leu Arg 345 ctc acc gac Leu Thr Asp tcc gac cac Ser Asp His cac cgc tac His Arg Tyr 395 cac tcg tgg	acc gcg ggt Thr Ala Gly 350 gcg gtc atc Ala Val Ile 365 cgg ctg ttc Arg Leu Phe 380 tcc ttc tac Ser Phe Tyr	His 335 cac 1296 His ggc 1344 Gly ctg 1440 Leu ctc 1488

420	425	430

		gac tgg cgt Asp Trp Arg 445	
		gcc gtc gcg Ala Val Ala 460	
		ggc agc gac Gly Ser Asp	
		ctg cga cgg Leu Arg Arg	
		acc gag gtc Thr Glu Val 510	
	 	gtc ggg cag Val Gly Gln 525	
 Gln Leu Pro	 JJ J J	acc gga atg Thr Gly Met 540	3
		tcg gtg gtt Ser Val Val	-
		tgc att acc Cys Ile Thr	
		cag ttc gcg Gln Phe Ala 590	
		gtg gtt acg Val Val Thr 605	
		cgt ttg gtg Arg Leu Val 620	
		gcg atc atc Ala Ile Ile	
		cac gga att His Gly Ile	

Gln Ile Ser Val Ala His Glu Trp Asp Cys Met Leu Arg Gly Gln Gln 660 665 670	256
acc gcg gaa ctg ggc gcg gga atc tac ctc cgg ccg gac gag gtc gat 2: Thr Ala Glu Leu Gly Ala Gly Ile Tyr Leu Arg Pro Asp Glu Val Asp 675 680 685	304
gcc gac tca ttg gcg agc gcc ctc acc cag gtg gtc gag gac ccc acc Ala Asp Ser Leu Ala Ser Ala Leu Thr Gln Val Val Glu Asp Pro Thr 690 695 700	352
tac acc gag aac gcg gtg aag ctt cgc gag gag gcg ctg tcc gac ccg Tyr Thr Glu Asn Ala Val Lys Leu Arg Glu Glu Ala Leu Ser Asp Pro 705 710 715	400
acg ccg cag gag atc gtc ccg cga ctg gag gaa ctc acg cgc cgc cac Thr Pro Gln Glu Ile Val Pro Arg Leu Glu Glu Leu Thr Arg Arg His 720 735 730 735	448
gcc ggc tagcggtttc cgaccgacaa gtccgtccga cagcacacct ccggagggag 2. Ala Gly	504
caggg atg tac gag ggc ggg ttc gcc gag ctt tac gac cgg ttc tac cgc 2 Met Tyr Glu Gly Gly Phe Ala Glu Leu Tyr Asp Arg Phe Tyr Arg 740 745 750	554
ggc cgg ggc aag gac tac gcg gcc gag gcc gcg cag gtc gcg cgg ctg 2 Gly Arg Gly Lys Asp Tyr Ala Ala Glu Ala Ala Gln Val Ala Arg Leu 755 760 765	602
	650
Val Arg Asp Arg Leu Pro Ser Ala Ser Ser Leu Leu Asp Val Ala Cys 770 775 780	
770 775 780	698
ggg acc ggc acc cac ctg cgc cgg ttc gcc gac ctc ttc gac gac gtg 2 Gly Thr Gly Thr His Leu Arg Arg Phe Ala Asp Leu Phe Asp Asp Val 785 790 795 800	
ggg acc ggc acc cac ctg cgc cgg ttc gcc gac ctc ttc gac gac gtg 2 Gly Thr Gly Thr His Leu Arg Arg Phe Ala Asp Leu Phe Asp Asp Val 785 790 795 800 acc ggg ctg gag ctg tcg gcg gcg atg atc gag gtc gcc cgg ccg cag 2 Thr Gly Leu Glu Leu Ser Ala Ala Met Ile Glu Val Ala Arg Pro Gln 805 810 815	698
ggg acc ggc acc cac ctg cgc cgg ttc gcc gac ctc ttc gac gac gtg 2 Gly Thr Gly Thr His Leu Arg Arg Phe Ala Asp Leu Phe Asp Asp Val 785 acc ggg ctg gag ctg tcg gcg gcg atg atc gac ggc ccg cag Thr Gly Leu Glu Leu Ser Ala Ala Met Ile Glu Val Ala Arg Pro Gln 805 ctc ggc ggc atc ccg gtg ctg cag ggc gac atg cgc gac ttc gcg ctg Leu Gly Gly Ile Pro Val Leu Gln Gly Asp Met Arg Asp Phe Ala Leu 820 825 780 2 2 2 2 2 2 3 3 4 5 6 7 7 7 7 7 7 7 7 7 7 7 7	698 746
ggg acc ggc acc cac ctg cgc cgg ttc gcc gac ctc ttc gac gac gtg 2 Gly Thr Gly Thr His Leu Arg Arg Phe Ala Asp Leu Phe Asp Asp Val 785 acc ggg ctg gag ctg tcg gcg gcg atg atc gac gtc gcc cgg ccg cag Thr Gly Leu Glu Leu Ser Ala Ala Met Ile Glu Val Ala Arg Pro Gln 805 ctc ggc ggc atc ccg gtg ctg cag ggc gac atg cgc gac ttc gcg ctg Leu Gly Gly Ile Pro Val Leu Gln Gly Asp Met Arg Asp Phe Ala Leu 820 gat cgc gag ttc gac gcc gtc acc tgc atg ttc agc tcc atc ggg cac Asp Arg Glu Phe Asp Ala Val Thr Cys Met Phe Ser Ser Ile Gly His 845	698 746 794

865	Pro Gly Gly 870	Val Val Val	Val Glu Pr 875	o Trp Trp Ph	e Pro 880
				g gtg cgc ga 1 Val Arg As 89	p Gly
		-	Ser Val Ar	ge gee gge gg g Ala Gly Gl 910	
				g gtg aac gg a Val Asn Gl 925	_
			-	c gag cgg ca e Glu Arg Gl	_
				g cag tac ct l Gln Tyr Le	
	tcc gga cgc Ser Gly Arg 965				3220
tgacccgtgc g	sttegegttt to	ccgttcctg go	acaggtga to	cgctccac ggg	ccctttc 3280
cccgccgtga c	ccggaccctt ac			atc gac aac Ile Asp Asn 980	gcc cgg 3334 Ala Arg
cgg cag caa	gcg gag ccg	Met A 975 tcg acg aca	rg Val Leu ccg cag gg	Ile Asp Asn 980 ga gag tcg at y Glu Ser Me	Ala Arg g ggt 3382
cgg cag caa Arg Gln Gln 985 gat cgg acc	gcg gag ccg Ala Glu Pro ggc gac cgg	Met A 975 tcg acg aca Ser Thr Thr 990 acg att ccg	rg Val Leu ccg cag gg Pro Gln Gl 99	Ile Asp Asn 980 ga gag tcg at y Glu Ser Me	Ala Arg g ggt 3382 t Gly a acg 3430
cgg cag caa Arg Gln Gln 985 gat cgg acc Asp Arg Thr 1000 cgt ttc ctg	gcg gag ccg Ala Glu Pro ggc gac cgg Gly Asp Arg 1005 ctc ggc gac	Met A 975 tcg acg aca Ser Thr Thr 990 acg att ccg Thr Ile Pro	ccg cag gg Pro Gln Gl gaa tcc tc Glu Ser Se 1010 ccc acc gc	Ile Asp Asn 980 ga gag tcg at y Glu Ser Me 95 gg cag acc gc	Ala Arg g ggt 3382 t Gly a acg 3430 a Thr 1015 a acc 3478 u Thr
cgg cag caa Arg Gln Gln 985 gat cgg acc Asp Arg Thr 1000 cgt ttc ctg Arg Phe Leu cac gac tgg His Asp Trp	gcg gag ccg Ala Glu Pro ggc gac cgg Gly Asp Arg 1005 ctc ggc gac Leu Gly Asp 1020 ctg acc cgc	Met A 975 tcg acg aca ser Thr Thr 990 acg att ccg Thr Ile Pro	ccg cag gg Pro Gln Gl gaa tcc tc Glu Ser Se 1010 ccc acc gc Pro Thr Al 1025 gag cag cg Glu Gln Ar	Ile Asp Asn 980 ga gag tcg at y Glu Ser Me 95 eg cag acc gc er Gln Thr Al ecc acg gcg ga a Thr Ala Gl	g ggt 3382 et Gly a acg 3430 a Thr 1015 a acc 3478 u Thr 0 g gcg 3526
cgg cag caa Arg Gln Gln 985 gat cgg acc Asp Arg Thr 1000 cgt ttc ctg Arg Phe Leu cac gac tgg His Asp Trp	gcg gag ccg Ala Glu Pro ggc gac cgg Gly Asp Arg 1005 ctc ggc gac Leu Gly Asp 1020 ctg acc cgc Leu Thr Arg	Met A 975 tcg acg aca Ser Thr Thr 990 acg att ccg Thr Ile Pro ggc gga atc Gly Gly Ile aac ggc gcc Asn Gly Ala 1040 atg gac cgc	ccg cag gg Pro Gln Gl gaa tcc tc Glu Ser Se 1010 ccc acc gc Pro Thr Al 1025 gag cag cg Glu Gln Ar	Ile Asp Asn 980 ga gag tcg at y Glu Ser Me 55 gg cag acc gc r Gln Thr Al cc acg gcg ga a Thr Ala Gl 103 gg ctc gag gt rg Leu Glu Va	Ala Arg g ggt 3382 et Gly a acg 3430 a Thr 1015 a acc 3478 u Thr 0 g gcg 3526 l Ala

cac gtg cgg acg aac ttc ggc tgg cgg cgg gac tgg atc cag ccc atc His Val Arg Thr Asn Phe Gly Trp Arg Arg Asp Trp Ile Gln Pro Ile 1080 1085 1090 1095	3670
atc gtg cag ccc gag atc ggc ttc ctc ggc ctc atc gtc aag gag ttc Ile Val Gln Pro Glu Ile Gly Phe Leu Gly Leu Ile Val Lys Glu Phe 1100 1105 1110	3718
gac ggt gtg ctg cac gtg ctg gcg cag gcc aag gcc gag ccg ggc aac Asp Gly Val Leu His Val Leu Ala Gln Ala Lys Ala Glu Pro Gly Asn 1115 1120 1125	3766
atc aac gcc gtc cag ctc tcc ccg acc ctg cag gcg acc cgc agc aac Ile Asn Ala Val Gln Leu Ser Pro Thr Leu Gln Ala Thr Arg Ser Asn 1130 1135 1140	3814
tac acc ggc gtc cac cgc ggc tcg aag gtc cgg ttc atc gag tac ttc Tyr Thr Gly Val His Arg Gly Ser Lys Val Arg Phe Ile Glu Tyr Phe 1145 1150 1155	3862
aac ggc acg cgc ccg agc cgg atc ctc gtc gac gtg ctc cag tcc gagAsn Gly Thr Arg Pro Ser Arg Ile Leu Val Asp Val Leu Gln Ser Glu1160116511701175	3910
cag ggc gcg tgg ttc ctg cgc aag cgc aac cgg aac atg gtc gtc gag Gln Gly Ala Trp Phe Leu Arg Lys Arg Asn Arg Asn Met Val Val Glu 1180 1185 1190	3958
gtg ttc gac gac ctg ccc gag cac ccg aac ttc cgg tgg ctg acc gtc Val Phe Asp Asp Leu Pro Glu His Pro Asn Phe Arg Trp Leu Thr Val 1195 1200 1205	4006
gcg cag ctg cgg gcg atg ctg cac cac gac aac gtg gtg aac atg gac Ala Gln Leu Arg Ala Met Leu His His Asp Asn Val Val Asn Met Asp 1210 1215 1220	4054
ctg cgc acc gtg ctg gcc tgc gtc ccg acc gcc gtg gag cgg gac cgg Leu Arg Thr Val Leu Ala Cys Val Pro Thr Ala Val Glu Arg Asp Arg 1225 1230 1235	4102
gcc gac gac gtg ctc gcg cgc ctg ccc gag ggc tcg ttc cag gcc cgg Ala Asp Asp Val Leu Ala Arg Leu Pro Glu Gly Ser Phe Gln Ala Arg 1240 1245 1250 1255	4150
ctg ctg cac tcg ttc atc ggc gcg ggc acc ccg gcc aac aac atg aac Leu Leu His Ser Phe Ile Gly Ala Gly Thr Pro Ala Asn Asn Met Asn 1260 1265 1270	4198
agc ctg ctg agc tgg atc tcc gac gtg cgc gcc agg cgc gag ttc gtg Ser Leu Leu Ser Trp Ile Ser Asp Val Arg Ala Arg Arg Glu Phe Val 1275 1280 1285	4246
cag cgc ggc cgc ccg ctg ccc gac atc gag cgc agc ggg tgg atc cgc Gln Arg Gly Arg Pro Leu Pro Asp Ile Glu Arg Ser Gly Trp Ile Arg 1290 1295 1300	4294
cgc gac gac ggc atc gag cac gag gag aag aag tac ttc gac gtc ttc	4342

Arg Asp Asp Gly Ile Glu His Glu Glu Lys Lys Tyr Phe Asp Val Phe 1305 1310 1315
ggc gtc acg gtg gcg acc agc gac cgc gag gtc aac tcg tgg atg cag 4390 Gly Val Thr Val Ala Thr Ser Asp Arg Glu Val Asn Ser Trp Met Gln 1320 1325 1330 1335
ccg ctg ctc tcg ccc gcc aac aac ggc ctg ctc gcc ctg ctg gtc aag Pro Leu Leu Ser Pro Ala Asn Asn Gly Leu Leu Ala Leu Leu Val Lys 1340 1345 1350
gac atc ggc ggc acg ttg cac gcg ctc gtg cag ctg cgc acc gag gcg 4486 Asp Ile Gly Gly Thr Leu His Ala Leu Val Gln Leu Arg Thr Glu Ala 1355 1360 1365
ggc ggg atg gac gtc gcc gag ctg gcg cct acg gtg cac tgc cag ccc 4534 Gly Gly Met Asp Val Ala Glu Leu Ala Pro Thr Val His Cys Gln Pro 1370 1375 1380
gac aac tac gcc gac gcg ccc gag gag ttc cga ccg gcc tat gtg gac 4582 Asp Asn Tyr Ala Asp Ala Pro Glu Glu Phe Arg Pro Ala Tyr Val Asp 1385 1390 1395
tac gtg ttg aac gtg ccg cgc tcg cag gtc cgc tac gac gca tgg cac Tyr Val Leu Asn Val Pro Arg Ser Gln Val Arg Tyr Asp Ala Trp His 1400 1405 1410 1415
tcc gag gag ggc ggc cgg ttc tac cgc aac gag aac cgg tac atg ctg 4678 Ser Glu Glu Gly Gly Arg Phe Tyr Arg Asn Glu Asn Arg Tyr Met Leu 1420 1430
atc gag gtg ccc gcc gac ttc gac gcc agt gcc gct ccc gac cac cgg 4726 Ile Glu Val Pro Ala Asp Phe Asp Ala Ser Ala Ala Pro Asp His Arg 1435 1440 1445
tgg atg acc ttc gac cag atc acc tac ctg ctc ggg cac agc cac tac 4774 Trp Met Thr Phe Asp Gln Ile Thr Tyr Leu Leu Gly His Ser His Tyr 1450 1455 1460
gtc aac atc cag ctg cgc agc atc atc gcg tgc gcc tcg gcc gtc tac 4822 Val Asn Ile Gln Leu Arg Ser Ile Ile Ala Cys Ala Ser Ala Val Tyr 1465 1470 1475
acc agg acc gcc gga tgaaacgcgc gctgaccgac ctggcgatct tcggcggccc 4877 Thr Arg Thr Ala Gly 1480
cgaggcattc ctgcacaccc tctacgtggg caggccgacc gtcggggacc gggagcggtt 4937
cttcgcccgc ctggagtggg cgctgaacaa caactggctg accaacggcg gaccactggt 4997
gcgcgagttc gagggccggg tcgccgacct ggcgggtgtc cgccactgcg tggccacctg 5057
caacgcgacg gtcgcgctgc aactggtgct gcgcgcgagc gacgtgtccg gcgaggtcgt 5117
catgccttcg atgacgttcg cggccaccgc gcacgcggcg agctggctgg ggctggaacc 5177

ggtgttctgc gacgtggacc ccgagaccgg cctgctcgac cccgagcacg tcgcgtcgct 5237 ggtgacaccg cggacggcg cgatcatcgg cgtgcacctg tggggcaggc ccgctccggt 5297 cgaggcgctg gagaagatcg ccgccgagca ccaggtcaaa ctcttcttcg acgccgcgca 5357 cgcgctgggc tgcaccgccg gcgggcggcc ggtcggcgcc ttcggcaacg ccgaggtgtt 5417 cagettecae gecaegaagg eggteacete gttegaggge ggegecateg teaecgaega 5477 cgggctgctg gccgaccgca tccgcgccat gcacaacttc gggatcgcac cggacaagct 5537 ggtgaccgat gtcggcacca acggcaagat gagcgagtgc gccgcggcga tgggcctcac 5597 ctcgctcgac gccttcgccg agaccagggt gcacaaccgc ctcaaccacg cgctctactc 5657 cgacgagete egegacgtge geggeatate egtgeacgeg ttegateetg gegageagaa 5717 caactaccag tacgtgatca tctcggtgga ctccgcggcc accggcatcg accgcgacca 5777 gttgcaggcg atcctgcgag cggagaaggt tgtggcacaa ccctacttct cccccgggtg 5837 ccaccagatg cagccgtacc ggaccgagcc gccgctgcgg ctggagaaca ccgaacagct 5897. ctccgaccgg gtgctcgcgc tgcccaccgg ccccgcggtg tccagcgagg acatccggcg 5957 ggtgtgcgac atcatccggc tcgccgccac cagcggcgag ctgatcaacg cgcaatggga 6017 ccagaggacg cgcaacggtt cgtgacgacc tgcgccacaa gtgccaggag gttcgctccc 6077 cg atg aac aca act cgt acg gca acc gcc cag gaa gcg ggg gtc gcc 6124 Met Asn Thr Thr Arg Thr Ala Thr Ala Gln Glu Ala Gly Val Ala 1490 gac gcg gcg cgc ccg gac gtc gac cgg cgg gcg gtc gtg cgg gcg ctg 6172 Asp Ala Ala Arg Pro Asp Val Asp Arg Arg Ala Val Arg Ala Leu 1505 1510 age teg gag gte tee ege gte ace gge gee ggt gae ggt gae gee gae 6220 Ser Ser Glu Val Ser Arg Val Thr Gly Ala Gly Asp Gly Asp Ala Asp 1520 1525 gtg cag gcc gcc cgg ctc gcc gac ctc gcc gcg cac tac ggg gcg cac 6268 Val Gln Ala Ala Arg Leu Ala Asp Leu Ala Ala His Tyr Gly Ala His 1540 ccg ttc acg ccg ctg gag cag acg cgt gcg cgg ctc ggc ctg gac cgc 6316 Pro Phe Thr Pro Leu Glu Gln Thr Arg Ala Arg Leu Gly Leu Asp Arg 1555 gcg gag ttc gcc cac ctg ctc gac ctg ttc ggc cgc atc ccg gac ctg 6364 Ala Glu Phe Ala His Leu Leu Asp Leu Phe Gly Arg Ile Pro Asp Leu 1570 ggc acc gcg gtg gag cac ggt ccg gcg ggc aag tac tgg tcc aac acg 6412 Gly Thr Ala Val Glu His Gly Pro Ala Gly Lys Tyr Trp Ser Asn Thr 1580 1585 1590 1595

atc aag ccg ctg gac gcc gca ggc gca ctg gac gcg gcg gtc tac cgc Ile Lys Pro Leu Asp Ala Ala Gly Ala Leu Asp Ala Ala Val Tyr Arg 1600 1605 1610	6460
aag cct gcc ttc ccc tac agc gtc ggc ctg tac ccc ggg ccg acg tgc Lys Pro Ala Phe Pro Tyr Ser Val Gly Leu Tyr Pro Gly Pro Thr Cys 1615 1620 1625	6508
atg ttc cgc tgc cac ttc tgc gtg cgg gtg acc ggt gcc cgc tac gag Met Phe Arg Cys His Phe Cys Val Arg Val Thr Gly Ala Arg Tyr Glu 1630 1635 1640	6556
gcc gca tcg gtc ccg gcg ggc aac gag acg ctg gcc gcg atc atc gac Ala Ala Ser Val Pro Ala Gly Asn Glu Thr Leu Ala Ala Ile Ile Asp 1645 1650 1655	6604
gag gtg ccc acg gac aac ccg aag gcg atg tac atg tcg ggc ggg ctc Glu Val Pro Thr Asp Asn Pro Lys Ala Met Tyr Met Ser Gly Gly Leu 1660 1665 1670 1675	6652
gag ccg ctg acc aac ccc ggt ctc ggc gag ctg gtg tcg cac gcc gcc Glu Pro Leu Thr Asn Pro Gly Leu Gly Glu Leu Val Ser His Ala Ala 1680 1685 1690	6700
ggg cgc ggt ttc gac ctc acc gtc tac acc aac gcc ttc gcc ctc acc Gly Arg Gly Phe Asp Leu Thr Val Tyr Thr Asn Ala Phe Ala Leu Thr 1695 1700 1705	6748
gag cag acg ctg aac cgc cag ccc ggc ctg tgg gag ctg ggc gcg atc Glu Gln Thr Leu Asn Arg Gln Pro Gly Leu Trp Glu Leu Gly Ala Ile 1710 1715 1720	6796
cgc acg tcc ctc tac ggg ctg aac aac gac gag tac gag acg acc acc Arg Thr Ser Leu Tyr Gly Leu Asn Asn Asp Glu Tyr Glu Thr Thr 1725 1730 1735	6844
ggc aag cgc ggc gct ttc gaa cgc gtc aag aag aac ctg cag ggc ttc Gly Lys Arg Gly Ala Phe Glu Arg Val Lys Lys Asn Leu Gln Gly Phe 1740 1745 1750 1755	6892
ctg cgg atg cgc gcc gag cgg gac gcg ccg atc cgg ctc ggc ttc aac Leu Arg Met Arg Ala Glu Arg Asp Ala Pro Ile Arg Leu Gly Phe Asn 1760 1765 1770	6940
cac atc atc ctg ccg gga cgg gcc gac cgg ctc acc gac ctc gtc gac His Ile Ile Leu Pro Gly Arg Ala Asp Arg Leu Thr Asp Leu Val Asp 1775 1780 1785	6988
ttc atc gcc gag ctc aac gag tcc agc ccg caa cgg ccg ctg gac ttc Phe Ile Ala Glu Leu Asn Glu Ser Ser Pro Gln Arg Pro Leu Asp Phe 1790 1795 1800	7036
gtg acg gtg cgc gag gac tac agc ggc cgc gac gac ggc cgg ctg tcg Val Thr Val Arg Glu Asp Tyr Ser Gly Arg Asp Asp Gly Arg Leu Ser	7084

gac tcc gag cgc aac gag ctg cgc gag ggc ctg gtg cgg ttc gtc gac Asp Ser Glu Arg Asn Glu Leu Arg Glu Gly Leu Val Arg Phe Val Asp 1820 1825 1830 1835	7132
tac gcc gcc gag cgg acc ccg ggc atg cac atc gac ctg ggc tac gcc Tyr Ala Ala Glu Arg Thr Pro Gly Met His Ile Asp Leu Gly Tyr Ala 1840 1845 1850	7180
ctg gag agc ctg cgg cgg ggt gtg gac gcc gag ctg ctg cgc atc cgg Leu Glu Ser Leu Arg Arg Gly Val Asp Ala Glu Leu Leu Arg Ile Arg 1855 1860 1865	7228
ccg gag acg atg cgt ccc acc gcg cac ccc cag gtc gcg gtg cag atc Pro Glu Thr Met Arg Pro Thr Ala His Pro Gln Val Ala Val Gln Ile 1870 1875 1880	7276
gac ctg ctc ggc gac gtc tac ctc tac cgc gag gcg ggc ttc ccg gag Asp Leu Leu Gly Asp Val Tyr Leu Tyr Arg Glu Ala Gly Phe Pro Glu 1885 1890 1895	7324
ctg gag ggc gcc acc cgc tac atc gcg ggc cgg gtc acc ccg tcg acc Leu Glu Gly Ala Thr Arg Tyr Ile Ala Gly Arg Val Thr Pro Ser Thr 1900 1905 1910 1915	7372
agc ctg cgc gag gtg gtg gag aac ttc gtg ctg gag aac gag ggc gtg Ser Leu Arg Glu Val Val Glu Asn Phe Val Leu Glu Asn Glu Gly Val 1920 1925 1930	7420
cag ccc cgc ccc ggc gac gag tac ttc ctc gac ggc ttc gac cag tcg Gln Pro Arg Pro Gly Asp Glu Tyr Phe Leu Asp Gly Phe Asp Gln Ser 1935 1940 1945	7468
gtg acc gca cgg ctc aac cag ctc gaa cga gac atc gcc gac ggg tgg Val Thr Ala Arg Leu Asn Gln Leu Glu Arg Asp Ile Ala Asp Gly Trp 1950 1955 1960	7516
gag gac cac cgc ggc ttc ctg cgc gga agg tgaaccggag ttgcgagtac Glu Asp His Arg Gly Phe Leu Arg Gly Arg 1965 1970	7566
gtgagctggc g gtg gcg ggt ttc gag ttc acc ccc gac ccg aag cag Met Ala Gly Gly Phe Glu Phe Thr Pro Asp Pro Lys Gln 1975 1980 1985	7616
gac cgg cgg ggc ctg ttc gtg tct ccg ctg cag gac gag gcg ttc gtg Asp Arg Arg Gly Leu Phe Val Ser Pro Leu Gln Asp Glu Ala Phe Val 1990 1995 2000	7664
ggc gcg gtg ggc cat cgg ttc ccc gtc gcc cag atg aac cac atc gtc Gly Ala Val Gly His Arg Phe Pro Val Ala Gln Met Asn His Ile Val 2005 2010 2015	7712
tec gee egg gge gtg etg ege ggg etg eac tte ace ace eeg eeg Ser Ala Arg Gly Val Leu Arg Gly Leu His Phe Thr Thr Pro Pro 2020 2025 2030	7760
ggg cag tgc aag tac gtc tac tgc gcg cgc ggc cgg gcg ctc gac gtc	7808

				•	
Gly Gln Cys I 2035	Lys Tyr Val 2040	Tyr Cys Ala	Arg Gly Arg 2045	_	Val 050
atc gtc gac a Ile Val Asp I	,	Gly Ser Pro			
gtg gag atg g Val Glu Met A 20					
acc gcg cac g Thr Ala His A 2085			Asp Asp Thr	-	
ctg gtc agc a Leu Val Ser 1 2100	Thr Pro Tyr				
ttc gac ccc g Phe Asp Pro A 2115				Leu Glu Val	
ctc tcc gac c Leu Ser Asp <i>F</i>		Val Ala Val			
cga ggg atg c Arg Gly Met I 21			Cys Leu Gly		
agc acc ggc a Ser Thr Gly A 2165					8160
<210> 7 <211> 322 <212> PRT <213> Sacchar	ropolyspora	erythraea			
				•	
<400> 7 Met Asn Gly 1	Ile Ser Asp 5	Ser Pro Arg	Gln Leu Ile 10	Thr Leu Leu 15	Gly
Ala Ser Gly I	Phe Val Gly 20	Ser Ala Val 25	_	Leu Arg Asp 30	His
Pro Val Arg I 35	Leu Arg Ala	Val Ser Arg	Gly Gly Ala	Pro Ala Val 45	Pro
Pro Gly Ala A 50	Ala Glu Val	Glu Asp Leu 55	Arg Ala Asp 60	Leu Leu Glu	Pro
Gly Arg Ala A 65	Ala Ala Ala 70	Ile Glu Asp	Ala Asp Val 75	Ile Val His	Leu 80

Val Ala His Ala Ala Gly Gly Ser Thr Trp Arg Ser Ala Thr Ser Asp Pro Glu Ala Glu Arg Val Asn Val Gly Leu Met His Asp Leu Val Gly 105 Ala Leu His Asp Arg Arg Ser Thr Pro Pro Val Leu Leu Tyr Ala 120 Ser Thr Ala Gln Ala Ala Asn Pro Ser Ala Ala Ser Arg Tyr Ala Gln 135 Gln Lys Thr Glu Ala Glu Arg Ile Leu Arg Lys Ala Thr Asp Glu Gly Arg Val Arg Gly Val Ile Leu Arg Leu Pro Ala Val Tyr Gly Gln Ser Gly Pro Ser Gly Pro Met Gly Arg Gly Val Val Ala Ala Met Ile Arg Arg Ala Leu Ala Gly Glu Pro Leu Thr Met Trp His Asp Gly Gly Val Arg Arg Asp Leu Leu His Val Glu Asp Val Ala Thr Ala Phe Ala Ala 215 220 Ala Leu Glu His His Asp Ala Leu Ala Gly Gly Thr Trp Ala Leu Gly Ala Asp Arg Ser Glu Pro Leu Gly Asp Ile Phe Arg Ala Val Ser Gly 250 Ser Val Ala Arg Gln Thr Gly Ser Pro Ala Val Asp Val Val Thr Val Pro Ala Pro Glu His Ala Glu Ala Asn Asp Phe Arg Ser Asp Asp Ile 280 Asp Ser Thr Glu Phe Arg Ser Arg Thr Gly Trp Arg Pro Arg Val Ser 290 Leu Thr Asp Gly Ile Asp Arg Thr Val Ala Ala Leu Thr Pro Thr Glu Glu His <210> 8 <211> 415 <212> PRT <213> Saccharopolyspora erythraea

Met Arg Val Leu Leu Thr Ser Phe Ala His Arg Thr His Phe Gln Gly

- 21 -

<400> 8

Leu Val Pro Leu Ala Trp Ala Leu Arg Thr Ala Gly His Asp Val Arg Val Ala Ala Gln Pro Ala Leu Thr Asp Ala Val Ile Gly Ala Gly Leu 40 Thr Ala Val Pro Val Gly Ser Asp His Arg Leu Phe Asp Ile Val Pro Glu Val Ala Ala Gln Val His Arg Tyr Ser Phe Tyr Leu Asp Phe Tyr 70 75 His Arg Glu Gln Glu Leu His Ser Trp Glu Phe Leu Leu Gly Met Gln Glu Ala Thr Ser Arg Trp Val Tyr Pro Val Val Asn Asn Asp Ser Phe Val Ala Glu Leu Val Asp Phe Ala Arg Asp Trp Arg Pro Asp Leu Val Leu Trp Glu Pro Phe Thr Phe Ala Gly Ala Val Ala Ala Arg Ala Cys 135 Gly Ala Ala His Ala Arg Leu Leu Trp Gly Ser Asp Leu Thr Gly Tyr Phe Arg Gly Arg Phe Gln Ala Gln Arg Leu Arg Arg Pro Pro Glu Asp 165 170 Arg Pro Asp Pro Leu Gly Thr Trp Leu Thr Glu Val Ala Gly Arg Phe Gly Val Glu Phe Gly Glu Asp Leu Ala Val Gly Gln Trp Ser Val Asp 200 Gln Leu Pro Pro Ser Phe Arg Leu Asp Thr Gly Met Glu Thr Val Val Ala Arg Thr Leu Pro Tyr Asn Gly Ala Ser Val Val Pro Asp Trp Leu Lys Lys Gly Ser Ala Thr Arg Arg Ile Cys Ile Thr Gly Gly Phe Ser Gly Leu Gly Leu Ala Ala Asp Ala Asp Gln Phe Ala Arg Thr Leu Ala Gln Leu Ala Arg Phe Asp Gly Glu Ile Val Val Thr Gly Ser Gly Pro 280 Asp Thr Ser Ala Val Pro Asp Asn Ile Arg Leu Val Asp Phe Val Pro

Met Gly Val Leu Gln Asn Cys Ala Ala Ile Ile His His Gly Gly

315

320

Ala Gly Thr Trp Ala Thr Ala Leu His His Gly Ile Pro Gln Ile Ser 325 330 335

Val Ala His Glu Trp Asp Cys Met Leu Arg Gly Gln Gln Thr Ala Glu 340 345 350

Leu Gly Ala Gly Ile Tyr Leu Arg Pro Asp Glu Val Asp Ala Asp Ser 355 360 365

Leu Ala Ser Ala Leu Thr Gln Val Val Glu Asp Pro Thr Tyr Thr Glu 370 375 380

Asn Ala Val Lys Leu Arg Glu Glu Ala Leu Ser Asp Pro Thr Pro Gln 385 390 395 400

Glu Ile Val Pro Arg Leu Glu Glu Leu Thr Arg Arg His Ala Gly
405 410 415

<210> 9

<211> 237

<212> PRT

<213> Saccharopolyspora erythraea

<400> 9

Met Tyr Glu Gly Gly Phe Ala Glu Leu Tyr Asp Arg Phe Tyr Arg Gly 1 5 10 15

Arg Gly Lys Asp Tyr Ala Ala Glu Ala Ala Gln Val Ala Arg Leu Val 20 25 30

Arg Asp Arg Leu Pro Ser Ala Ser Ser Leu Leu Asp Val Ala Cys Gly 35 40 45

Thr Gly Thr His Leu Arg Arg Phe Ala Asp Leu Phe Asp Asp Val Thr 50 55 60

Gly Leu Glu Leu Ser Ala Ala Met Ile Glu Val Ala Arg Pro Gln Leu 65 70 75 80

Gly Gly Ile Pro Val Leu Gln Gly Asp Met Arg Asp Phe Ala Leu Asp 85 90 95

Arg Glu Phe Asp Ala Val Thr Cys Met Phe Ser Ser Ile Gly His Met 100 105 110

Arg Asp Gly Ala Glu Leu Asp Gln Ala Leu Ala Ser Phe Ala Arg His
115 120 125

Leu Ala Pro Gly Gly Val Val Val Glu Pro Trp Trp Phe Pro Glu
130 135 140

Asp Phe Leu Asp Gly Tyr Val Ala Gly Asp Val Val Arg Asp Gly Asp 145 150 155 160

Leu Thr Ile Ser Arg Val Ser His Ser Val Arg Ala Gly Gly Ala Thr 165 170 175 Arg Met Glu Ile His Trp Val Val Ala Asp Ala Val Asn Gly Pro Arg 180 185 190

His His Val Glu His Tyr Glu Ile Thr Leu Phe Glu Arg Gln Gln Tyr 195 200 205

Glu Lys Ala Phe Thr Ala Ala Gly Cys Ala Val Gln Tyr Leu Glu Gly 210 215 220

Gly Pro Ser Gly Arg Gly Leu Phe Val Gly Val Arg Gly 225 230 235

<210> 10

<211> 510

<212> PRT

<213> Saccharopolyspora erythraea

<400> 10

Met Arg Val Leu Ile Asp Asn Ala Arg Arg Gln Gln Ala Glu Pro Ser 1 5 10 15

Thr Thr Pro Gln Gly Glu Ser Met Gly Asp Arg Thr Gly Asp Arg Thr 20 25 30

Ile Pro Glu Ser Ser Gln Thr Ala Thr Arg Phe Leu Leu Gly Asp Gly 35 40 45

Gly Ile Pro Thr Ala Thr Ala Glu Thr His Asp Trp Leu Thr Arg Asn 50 55 60

Gly Ala Glu Gln Arg Leu Glu Val Ala Arg Val Pro Phe Ser Ala Met 65 70 75 80

Asp Arg Trp Ser Phe Gln Pro Glu Asp Gly Arg Leu Ala His Glu Ser 85 90 95

Gly Arg Phe Phe Ser Ile Glu Gly Leu His Val Arg Thr Asn Phe Gly 100 105 110

Trp Arg Arg Asp Trp Ile Gln Pro Ile Ile Val Gln Pro Glu Ile Gly
115 120 125

Phe Leu Gly Leu Ile Val Lys Glu Phe Asp Gly Val Leu His Val Leu 130 135 140

Ala Gln Ala Lys Ala Glu Pro Gly Asn Ile Asn Ala Val Gln Leu Ser 145 150 155 160

Pro Thr Leu Gln Ala Thr Arg Ser Asn Tyr Thr Gly Val His Arg Gly
165 170 175

Ser Lys Val Arg Phe Ile Glu Tyr Phe Asn Gly Thr Arg Pro Ser Arg 180 185 190

Ile Leu Val Asp Val Leu Gln Ser Glu Gln Gly Ala Trp Phe Leu Arg

195 200 205

Lys Arg Asn Arg Asn Met Val Val Glu Val Phe Asp Asp Leu Pro Glu

210 215 220

His Pro Asn Phe Arg Trp Leu Thr Val Ala Gln Leu Arg Ala Met Leu 225 230 235 240

His His Asp Asn Val Val Asn Met Asp Leu Arg Thr Val Leu Ala Cys 245 250 255

Val Pro Thr Ala Val Glu Arg Asp Arg Ala Asp Asp Val Leu Ala Arg 260 265 270

Leu Pro Glu Gly Ser Phe Gln Ala Arg Leu Leu His Ser Phe Ile Gly
275 280 285

Ala Gly Thr Pro Ala Asn Asn Met Asn Ser Leu Leu Ser Trp Ile Ser 290 295 300

Asp Val Arg Ala Arg Glu Phe Val Gln Arg Gly Arg Pro Leu Pro 305 310 315 320

Asp Ile Glu Arg Ser Gly Trp Ile Arg Asp Asp Gly Ile Glu His 325 330 335

Glu Glu Lys Lys Tyr Phe Asp Val Phe Gly Val Thr Val Ala Thr Ser 340 345 350

Asp Arg Glu Val Asn Ser Trp Met Gln Pro Leu Leu Ser Pro Ala Asn 355 360 365

Asn Gly Leu Leu Ala Leu Leu Val Lys Asp Ile Gly Gly Thr Leu His 370 375 380

Ala Leu Val Gln Leu Arg Thr Glu Ala Gly Gly Met Asp Val Ala Glu 385 390 395 400

Leu Ala Pro Thr Val His Cys Gln Pro Asp Asn Tyr Ala Asp Ala Pro 405 410 415

Glu Glu Phe Arg Pro Ala Tyr Val Asp Tyr Val Leu Asn Val Pro Arg 420 425 430

Ser Gln Val Arg Tyr Asp Ala Trp His Ser Glu Glu Gly Gly Arg Phe 435 440 445

Tyr Arg Asn Glu Asn Arg Tyr Met Leu Ile Glu Val Pro Ala Asp Phe 450 455 460

Asp Ala Ser Ala Ala Pro Asp His Arg Trp Met Thr Phe Asp Gln Ile 465 470 475 480

Thr Tyr Leu Leu Gly His Ser His Tyr Val Asn Ile Gln Leu Arg Ser 485 490 495

Ile Ile Ala Cys Ala Ser Ala Val Tyr Thr Arg Thr Ala Gly

500 505 510

<210> 11 <211> 489 <212> PRT <213> Saccharopolyspora erythraea Met Asn Thr Thr Arg Thr Ala Thr Ala Gln Glu Ala Gly Val Ala Asp Ala Ala Arg Pro Asp Val Asp Arg Ala Val Val Arg Ala Leu Ser · Ser Glu Val Ser Arg Val Thr Gly Ala Gly Asp Gly Asp Ala Asp Val Gln Ala Ala Arg Leu Ala Asp Leu Ala Ala His Tyr Gly Ala His Pro Phe Thr Pro Leu Glu Gln Thr Arg Ala Arg Leu Gly Leu Asp Arg Ala Glu Phe Ala His Leu Leu Asp Leu Phe Gly Arg Ile Pro Asp Leu Gly Thr Ala Val Glu His Gly Pro Ala Gly Lys Tyr Trp Ser Asn Thr Ile Lys Pro Leu Asp Ala Ala Gly Ala Leu Asp Ala Ala Val Tyr Arg Lys 120 Pro Ala Phe Pro Tyr Ser Val Gly Leu Tyr Pro Gly Pro Thr Cys Met 130 Phe Arg Cys His Phe Cys Val Arg Val Thr Gly Ala Arg Tyr Glu Ala 150 155 Ala Ser Val Pro Ala Gly Asn Glu Thr Leu Ala Ala Ile Ile Asp Glu Val Pro Thr Asp Asn Pro Lys Ala Met Tyr Met Ser Gly Gly Leu Glu Pro Leu Thr Asn Pro Gly Leu Gly Glu Leu Val Ser His Ala Ala Gly Arg Gly Phe Asp Leu Thr Val Tyr Thr Asn Ala Phe Ala Leu Thr Glu

Gln Thr Leu Asn Arg Gln Pro Gly Leu Trp Glu Leu Gly Ala Ile Arg

Thr Ser Leu Tyr Gly Leu Asn Asn Asp Glu Tyr Glu Thr Thr Thr Gly 245 250 255

Lys Arg Gly Ala Phe Glu Arg Val Lys Lys Asn Leu Gln Gly Phe Leu

260 265 270

Arg Met Arg Ala Glu Arg Asp Ala Pro Ile Arg Leu Gly Phe Asn His 275 280 285

Ile Ile Leu Pro Gly Arg Ala Asp Arg Leu Thr Asp Leu Val Asp Phe 290 295 300

Ile Ala Glu Leu Asn Glu Ser Ser Pro Gln Arg Pro Leu Asp Phe Val 305 310 315 320

Thr Val Arg Glu Asp Tyr Ser Gly Arg Asp Asp Gly Arg Leu Ser Asp 325 330 335

Ser Glu Arg Asn Glu Leu Arg Glu Gly Leu Val Arg Phe Val Asp Tyr 340 345 350

Ala Ala Glu Arg Thr Pro Gly Met His Ile Asp Leu Gly Tyr Ala Leu 355 360 365

Glu Ser Leu Arg Arg Gly Val Asp Ala Glu Leu Leu Arg Ile Arg Pro 370 375 380

Glu Thr Met Arg Pro Thr Ala His Pro Gln Val Ala Val Gln Ile Asp 385 390 395 400

Leu Leu Gly Asp Val Tyr Leu Tyr Arg Glu Ala Gly Phe Pro Glu Leu 405 410 415

Glu Gly Ala Thr Arg Tyr Ile Ala Gly Arg Val Thr Pro Ser Thr Ser 420 425 430

Leu Arg Glu Val Val Glu Asn Phe Val Leu Glu Asn Glu Gly Val Gln 435 440 445

Pro Arg Pro Gly Asp Glu Tyr Phe Leu Asp Gly Phe Asp Gln Ser Val 450 455 460

Thr Ala Arg Leu Asn Gln Leu Glu Arg Asp Ile Ala Asp Gly Trp Glu 465 470 475 480

Asp His Arg Gly Phe Leu Arg Gly Arg 485

<210> 12

<211> 193

<212> PRT

<213> Saccharopolyspora erythraea

<400> 12

Met Ala Gly Gly Phe Glu Phe Thr Pro Asp Pro Lys Gln Asp Arg Arg 1 5 10 15

Gly Leu Phe Val Ser Pro Leu Gln Asp Glu Ala Phe Val Gly Ala Val
20 25 30

Gly His Arg Phe Pro Val Ala Gln Met Asn His Ile Val Ser Ala Arg 40 Gly Val Leu Arg Gly Leu His Phe Thr Thr Pro Pro Gly Gln Cys Lys Tyr Val Tyr Cys Ala Arg Gly Arg Ala Leu Asp Val Ile Val Asp 70 Ile Arg Val Gly Ser Pro Thr Phe Gly Lys Trp Asp Ala Val Glu Met Asp Thr Glu His Phe Arq Ala Val Tyr Phe Pro Arg Gly Thr Ala His 100 105 Ala Phe Leu Ala Leu Glu Asp Asp Thr Leu Met Ser Tyr Leu Val Ser Thr Pro Tyr Val Ala Glu Tyr Glu Gln Ala Ile Asp Pro Phe Asp Pro Ala Leu Gly Leu Pro Trp Pro Ala Asp Leu Glu Val Val Leu Ser Asp 155 Arg Asp Thr Val Ala Val Asp Leu Glu Thr Ala Arg Arg Arg Gly Met 165 170 Leu Pro Asp Tyr Ala Asp Cys Leu Gly Glu Pro Ala Ser Thr Gly 185 Arg <210> 13 <211> 1206 <212> DNA <213> Saccharopolyspora erythraea <220> <221> CDS <222> (1)..(1203) <223> /function= "involved in the biosynthesis of desosamine" /gene= "eryCIV" /note= "SEQ ID No 6 from 4837 to 6039" <220> <221> mat_peptide <222> (1) <400> 13L atg aaa ege geg etg ace gae etg geg ate tte gge gge eee gag gea Met Lys Arg Ala Leu Thr Asp Leu Ala Ile Phe Gly Gly Pro Glu Ala 10 ttc ctg cac acc ctc tac gtg ggc agg ccg acc gtc ggg gac cgg gag 96 Phe Leu His Thr Leu Tyr Val Gly Arg Pro Thr Val Gly Asp Arg Glu 20 25

											tgg Trp			144
											gcc Ala			192
											gtc Val			240
											gtc Val			288
											ctg Leu 110			336
											ctc Leu			384
											atc Ile			432
											gag Glu			480
_	_			_	_				_	_	 cac His		_	528
											aac Asn 190			576
											gag Glu			624
											cgc Arg			672
											gtc Val			720
		_	_	_		_	_	 	_		acc Thr	_		768

_	_		_				cac His 265		_						816
		_		_	_		cgc Arg								864
							cag Gln								912
		_			_	_	gac Asp	_	_	_			_	_	960
		_	_	 _			tac Tyr					_		_	1008
_	_	_				_	ccg Pro 345	_		_					1056
							ctg Leu								1104
							gac Asp								1152
_			_				tgg Trp	_	_		_	_			1200
tcg Ser	tga			-											1206
)> 14														
<21	L> 4()1													

<211> 401

<212> PRT

<213> Saccharopolyspora erythraea

<400> 14

Met Lys Arg Ala Leu Thr Asp Leu Ala Ile Phe Gly Gly Pro Glu Ala 5

Phe Leu His Thr Leu Tyr Val Gly Arg Pro Thr Val Gly Asp Arg Glu

Arg Phe Phe Ala Arg Leu Glu Trp Ala Leu Asn Asn Asn Trp Leu Thr 40

Asn Gly Gly Pro Leu Val Arg Glu Phe Glu Gly Arg Val Ala Asp Leu 50 55

- 30 -

Ala Gly Val Arg His Cys Val Ala Thr Cys Asn Ala Thr Val Ala Leu Gln Leu Val Leu Arg Ala Ser Asp Val Ser Gly Glu Val Val Met Pro 90 Ser Met Thr Phe Ala Ala Thr Ala His Ala Ala Ser Trp Leu Gly Leu 105 Glu Pro Val Phe Cys Asp Val Asp Pro Glu Thr Gly Leu Leu Asp Pro 115 120 Glu His Val Ala Ser Leu Val Thr Pro Arg Thr Gly Ala Ile Ile Gly Val His Leu Trp Gly Arg Pro Ala Pro Val Glu Ala Leu Glu Lys Ile Ala Ala Glu His Gln Val Lys Leu Phe Phe Asp Ala Ala His Ala Leu 170 Gly Cys Thr Ala Gly Gly Arg Pro Val Gly Ala Phe Gly Asn Ala Glu Val Phe Ser Phe His Ala Thr Lys Ala Val Thr Ser Phe Glu Gly Gly 200 Ala Ile Val Thr Asp Asp Gly Leu Leu Ala Asp Arg Ile Arg Ala Met His Asn Phe Gly Ile Ala Pro Asp Lys Leu Val Thr Asp Val Gly Thr 230 235 Asn Gly Lys Met Ser Glu Cys Ala Ala Met Gly Leu Thr Ser Leu 250 Asp Ala Phe Ala Glu Thr Arg Val His Asn Arg Leu Asn His Ala Leu 265 Tyr Ser Asp Glu Leu Arg Asp Val Arg Gly Ile Ser Val His Ala Phe 275 Asp Pro Gly Glu Gln Asn Asn Tyr Gln Tyr Val Ile Ile Ser Val Asp Ser Ala Ala Thr Gly Ile Asp Arg Asp Gln Leu Gln Ala Ile Leu Arg Ala Glu Lys Val Val Ala Gln Pro Tyr Phe Ser Pro Gly Cys His Gln Met Gln Pro Tyr Arg Thr Glu Pro Pro Leu Arg Leu Glu Asn Thr Glu 345 Gln Leu Ser Asp Arg Val Leu Ala Leu Pro Thr Gly Pro Ala Val Ser 355 360 365

```
Ser Glu Asp Ile Arg Arg Val Cys Asp Ile Ile Arg Leu Ala Ala Thr
    370
                        375
Ser Gly Glu Leu Ile Asn Ala Gln Trp Asp Gln Arg Thr Arg Asn Gly
                                         395
385
                    390
                                                             400
Ser
<210> 15
<211> 6093
<212> DNA
<213> Streptomyces antibioticus
<220>
<221> CDS
<222> (184)..(1386)
<223> /gene= "oleP1"
<220>
<221> CDS
<222> (1437)..(2714)
<223> /function= "glycosylation of 8,
      8a-desoxyoleandolide" /gene= "oleG1"
      /transl_except= (pos: 1437...1439, aa: Met)
<220>
<221> CDS
<222> (2722)..(3999)
<223> /function= "glycosylation of 8,
      8a-desoxyoleandolide" /gene= "oleG2"
<220>
<221> CDS
<222> (4810)..(5967)
<223> /gene= "oleY"
<220>
<221> mat_peptide
<222> (184)
<400> 15
gcatgccccg ctttcctccc cctctccqaa cgcatcgacg acccgatccc cctcaqggac 60
cggtgaagga gcgtgttgca ctcatgcagg acatgcaagg cgtacagccc gaaccagcca 120
gtgtcgaaca cgcggcggac gcagctcgaa cagagcgaac ggcgcacgga agccgcccag 180
gag atg gag gac agc gaa ctg ggg cgc cgc ctg cag atg ctc cgc ggc
    Met Glu Asp Ser Glu Leu Gly Arg Arg Leu Gln Met Leu Arg Gly
      1
atg cag tgg gtc ttc ggc gcc aac ggc gat ccg tac gcc cgg ctg ctg
                                                                    276
Met Gln Trp Val Phe Gly Ala Asn Gly Asp Pro Tyr Ala Arg Leu Leu
                 20
```

_		_		_	_	_		cct Pro 40			_					324
								acc Thr								372
								gcc Ala								420
								aag Lys								468
	_				_			ctg Leu		_		_			_	516
		_			_			ccg Pro 120		_		_			-	564
								gag Glu								612
								gtc Val								660
								tgg Trp								708
								gcg Ala								756
								ctg Leu 200								804
								gac Asp								852
								gga Gly								900
								acc Thr								948
ctc	ggg	ctc	ctt	ccc	aaa	cag	tgg	ccc	gtg	ccc	tgc	acc	ggc	cgg	gtg	996

- 33 -

. .

579914_1

Leu	Gly	Leu	Leu	Pro 260	Gly	Gln	Trp	Pro	Val 265	Pro	Cys	Thr	Gly	Arg 270	Val	
-	gcc Ala													-		1044
	atc Ile															1092
	gtc Val 305															1140
	aac Asn		_		_	_	-	_		_		_				1188
_	ccg Pro		_	_	_	_			_	Āla	_					1236
_	gcc Ala	_			_		-		_			_		_	_	1284
	gcg Ala						_	_								1332
	cgg Arg 385															1380
_	gca Ala	tgag	gcato	cgc (gtcga	aacg	gc go	cgcgo	ctcg	g cc	ccc	gccg	gcc	cctgo	ege	1436
	atg Met					_	_		_							1484
	ctg Leu														gtg Val	1532
	cag Gln 435															1580
	ccg Pro															1628
	gac Asp															1676

	470	475	480	•
	tgg acg tgg cc Trp Thr Trp Pr			
	ttc tac gag tt Phe Tyr Glu Le 50	eu Leu Asn Asn		_
	ttc gcc cgt ga Phe Ala Arg As 520			
	ttc gcc ggc gc Phe Ala Gly Al 535			
	g ctg ccg tgg gg g Leu Pro Trp Gl 550			Arg
5 5 5	gcc gag cgt gc Ala Glu Arg Al	cc ctg caa ccg	J J J	
	gag tgg ctg gg Glu Trp Leu Gl 58	ly Arg Met Leu		_
	g gag atg gtc ac Glu Met Val Th 600			_
	g cgg ctg gag ct : Arg Leu Glu Le 615			•
	g ccg tac aac gg . Pro Tyr Asn Gl 630		-	Val
	gag cgg ccc cg Glu Arg Pro Ar			
	ggc cgg gac ca Gly Arg Asp Hi 66			
	gtg gac gcg ga Val Asp Ala Gl 680			
	c ctg cgg ggc gc g Leu Arg Gly Al 695			

gac t Asp P																2396
cac c His H				_		_		_	_						_	2444
ccg c Pro G	3ln			_	_		_		_		_				_	2492
cgc a Arg M	_							_	_	_	_	_		_	_	2540
ggc g Gly V 770																2588
gag t Glu P																2636
ccc g Pro A	_			_	_	_	_	_	_	_	_					2684
cat g His A	Ala										gacg			gta Val 830		2733
	Ala	Thr 820 tgc	Gly	Ala gcc	Met	Ala	Gly 825 acc	Arg	Arg ttc	cac	a gg	Met ctg	Arg gtg	Val 830 ccg	Leu	2733 2781
His A	acc Thr	Thr 820 tgc Cys	ttc Phe 835 ctg	Ala gcc Ala cgg	Met aac Asn gcc	Ala gac Asp	Gly 825 acc Thr	cac His 840	Arg ttc Phe gaa	cac His	cgc Gly aaa	Met ctg Leu	Arg gtg Val 845 gcc	Val 830 ccg Pro	ctg Leu	
ctg a Leu T gcg t Ala T ccc g	Ala acc Thr tgg Trp	Thr 820 tgc Cys gcg Ala 850 ctg	ttc Phe 835 ctg Leu	Ala gcc Ala cgg Arg	Met aac Asn gcc Ala acg	Ala gac Asp gcc Ala	Gly 825 acc Thr ggg Gly 855 acc	cac His 840 cac His	Arg ttc Phe gaa Glu	cac His gtc Val	ggg Gly cgc Arg	ctg Leu gtg Val 860	gtg Val 845 gcc Ala	Val 830 ccg Pro agt Ser	ctg Leu cag Gln	2781
ctg a Leu T gcg t Ala T ccc g	Ala acc Thr tgg Trp gcc Ala 865	Thr 820 tgc Cys gcg Ala 850 ctg Leu	ttc Phe 835 ctg Leu tcc Ser	Ala gcc Ala cgg Arg gac Asp	Met aac Asn gcc Ala acg Thr	gac Asp gcc Ala atc Ile 870	Gly 825 acc Thr ggg Gly 855 acc Thr	cac His 840 cac His caa Gln	ttc Phe gaa Glu gcg Ala	cac His gtc Val gga Gly	ggg Gly cgc Arg ctg Leu 875	ctg Leu gtg Val 860 acc Thr	gtg Val 845 gcc Ala gcg Ala	Val 830 ccg Pro agt Ser gtg Val	ctg Leu cag Gln ccc Pro	2781 2829
ctg a Leu T gcg t Ala T ccc g Pro A gtg g Val G	Ala acc Thr tgg Trp gcc Ala 865 ggc Gly	tgc Cys gcg Ala 850 ctg Leu cgg Arg	ttc Phe 835 ctg Leu tcc Ser gac Asp	Ala gcc Ala cgg Arg gac Asp acc Thr	Met aac Asn gcc Ala acg Thr gcc Ala 885	gac Asp gcc Ala atc Ile 870 ttc Phe	Gly 825 acc Thr ggg Gly 855 acc Thr ctg Leu	cac His 840 cac His caa Gln gag Glu	ttc Phe gaa Glu gcg Ala ctg Leu	cac His gtc Val gga Gly atg Met 890 ctg	ggg Gly cgc Arg ctg Leu 875 ggg Gly	Met ctg Leu gtg Val 860 acc Thr	gtg Val 845 gcc Ala gcg Ala atc	Val 830 ccg Pro agt Ser gtg Val ggc Gly	ctg Leu cag Gln ccc Pro gcg Ala 895	2781 2829 2877

acg ttc tac tcg Thr Phe Tyr Ser 930					3069
gcg ctg acc cgg Ala Leu Thr Arg 945		_		· -	3117
agc ttc gcc ggg Ser Phe Ala Gly 960					3165
cgc gtg ctg tgg Arg Val Leu Trp					3213
ctc gcg gag cgg Leu Ala Glu Arg 995	Ala Asn Arg		His Arg Glu A		3261
gcg gag tgg ctg Ala Glu Trp Leu 1010	Gly Trp Ala				3309
gag gag ctg gtg Glu Glu Leu Val 1025		Trp Thr Ile			3357
atg cgg ctg ccc Met Arg Leu Pro 1040		Thr Thr Val			3405
tac aac ggg cgg Tyr Asn Gly Arg					3453
cgg ccc cgg atc Arg Pro Arg Ile 1075	Cys Leu Thr		Ser Ala Arg (_	3501
ggc gac ggc gtg Gly Asp Gly Val 1090	Ser Leu Ala				3549
gac gcg gag atc Asp Ala Glu Ile 1105					3597
ggg ccg gtg ccg Gly Pro Val Pro 1120		Arg Leu Val			3645
gcc ctg atg ccg Ala Leu Met Pro					3693
acc tgg ctg acg	gcc gcc gtc	cac ggc gtc	ccg cag atc o	gtc ctc ggt	3741

Thr Trp Leu Thr Ala Ala Val His Gly Val Pro Gln Ile Val Leu Gly 1155 1160 1165	
gac ctc tgg gac aac ctg ctg cgc gcc cgg cag aca cag gcc gcg ggc Asp Leu Trp Asp Asn Leu Leu Arg Ala Arg Gln Thr Gln Ala Ala Gly 1170 1175 1180	3789
gcg ggc ctg ttc atc cat ccg tcc gag gtc acc gcg gcc ggg ctc ggt Ala Gly Leu Phe Ile His Pro Ser Glu Val Thr Ala Ala Gly Leu Gly 1185 1190 1195	3837
gag ggc gtg cgc cgg gtg ctg acg gac cct tcc atc cgg gcc gcc gca Glu Gly Val Arg Arg Val Leu Thr Asp Pro Ser Ile Arg Ala Ala Ala 1200 1205 1210 1215	3885
cag cgc gtc cgg gac gag atg aat gca gag ccg acg ccg ggc gag gtc Gln Arg Val Arg Asp Glu Met Asn Ala Glu Pro Thr Pro Gly Glu Val 1220 1225 1230	3933
gtc acg gtg ctg gag cgg ctc gcc gcg agc ggc gga cgc gga cga gga Val Thr Val Leu Glu Arg Leu Ala Ala Ser Gly Gly Arg Gly Arg Gly 1235 1240 1245	3981
ggc ggg aac cat gcg ggc tgacacggag ccgaccaccg ggtacgagga Gly Gly Asn His Ala Gly 1250	4029
cgagttcgcc gagatctacg acgccgtgta ccggggccgg ggcaaggact acgccggcga	4089
ggcgaaggac gtggcggacc tcgtgcgcga ccgggtgccg gacgcgtcct ccctcctgga	4149
cgtggcctgc ggcacgggcg cgcacctgcg gcacttcgcc acgctcttcg acgacgcccg	4209
cggtctcgaa ctgtccgcga gcatgctgga catcgcccgc tcccgcatgc cgggcgtgcc	4269
gctgcaccaa ggggacatgc gatccttcga cctggggcca cgcgtctccg cggtcacctg	4329
catgttcagc tccgtcggcc acctggccac caccgccgaa ctcgacgcga cgctgcggtg	4389
cttcgcccgg cacacccggc ccggcggcgt ggccgtcatc gaaccgtggt ggttcccgga	4449
gaccttcacc gacggctacg tggcgggtga catcgtacgc gtcgacggcc ggaccatctc	4509
ccgggtgtcc cactcggtac gggacggcgg cgccacccgc atggagatcc actacgtgat	4569
cgccgacgcc gagcacggtc cccggcacct ggtcgagcac caccgcatca cgctgttccc	4629
geggeatgeg tacaeggeeg egtaegagaa ggegggetae acegtegagt acetegaegg	4689
cgggccctcg ggccgggggc tgttcgtcgg cacccggacg tgaacccgcc cgcgcaccgc	4749
ccgatcaccc tgctcaacgc cgttcacacg gatcaccgga ccacgcgaag gacctttcac	4809
atg tcg tac gac gac cac gcg gtg ctg gaa gcg ata ctg cgg tgc gcc Met Ser Tyr Asp Asp His Ala Val Leu Glu Ala Ile Leu Arg Cys Ala 1255 1260 1265	4857

gga ggt gac gag cgc Gly Gly Asp Glu Arg 1270 1			
gcc gag atc acc gcg Ala Glu Ile Thr Ala 1290	Ala Leu Val Asp		
atc ccg cag gtg ggc Ile Pro Gln Val Gly 1305		Ile Gly Leu Asp	
ggc gcc gac cgg atc Gly Ala Asp Arg Ile 1320			
gtc acg tcg gcg gaa Val Thr Ser Ala Glu 1335			
agt tca cgc tca gcg Ser Ser Arg Ser Ala 1350			
ggc cgc acc gcg ggg Gly Arg Thr Ala Gly 1370	Gly Phe Gly Val		
ggc ccg cgg acc atg Gly Pro Arg Thr Met 1385		Leu Ala Ala Arg	
gtg gtg ctg cac gcg Val Val Leu His Ala 1400			
gcc ctg cgc tac gag Ala Leu Arg Tyr Glu 1415			
ggc cac tac gac cgg Gly His Tyr Asp Arg 1430			
atc ctg gag atc ggc Ile Leu Glu Ile Gly 1450	Ile Gly Gly Tyr		
gcc tca ctg aag atg Ala Ser Leu Lys Met 1465		Phe Pro Arg Gly	
ggc gtg gac atc ttc Gly Val Asp Ile Phe 1480			
cgc tcc gcg gcc cgg	cag gac gac ccg	gag ttc atg cgc	cgc gtc gcc 5577

Arg Ser Ala Ala Arg Gln Asp Asp Pro Glu Phe Met Arg Arg Val Ala 1495 1500 1505	
gag gag cac ggg ccg ttc gac gtc atc atc gac gac ggc agc cac atc Glu Glu His Gly Pro Phe Asp Val Ile Ile Asp Asp Gly Ser His Ile 1510 1515 1520 1525	5
aac gca cac atg cgg acg tcg ttc tcg gtg atg ttc ccc cac ctg cgc 567 Asn Ala His Met Arg Thr Ser Phe Ser Val Met Phe Pro His Leu Arg 1530 1535 1540	3
aac ggc ggc ttc tac gtc atc gag gac acc ttc acc tcc tac tgg ccc 572 Asn Gly Gly Phe Tyr Val Ile Glu Asp Thr Phe Thr Ser Tyr Trp Pro 1545 1550 1555	1
ggg tac gga ggg cca tcc gga gcc cgg tgc ccg tcc gga aca acc gcg 576 Gly Tyr Gly Gly Pro Ser Gly Ala Arg Cys Pro Ser Gly Thr Thr Ala 1560 1565 1570	9
ctg gag atg gtc aag gga ctg atc gac tcg gtg cac tac gag gag cgg 581 Leu Glu Met Val Lys Gly Leu Ile Asp Ser Val His Tyr Glu Glu Arg 1575 1580 1585	7 .
ccg gac ggc gcg gcc acg gcc gac tac atc gcc agg aac ctc gtc ggg Pro Asp Gly Ala Ala Thr Ala Asp Tyr Ile Ala Arg Asn Leu Val Gly 1590 1595 1600 1605	5
ctg cac gcc tac caa acg acc tcg tct tcc tcg aga agg gcg atc aac 591 Leu His Ala Tyr Gln Thr Thr Ser Ser Ser Arg Arg Ala Ile Asn 1610 1615 1620	3
aag gag ggc ggc atc ccc cac acc gtg ccc cgg gag ccg ttc tgg aac 596 Lys Glu Gly Gly Ile Pro His Thr Val Pro Arg Glu Pro Phe Trp Asn 1625 1630 1635	1
gac aac tagccacggc cgcaaccaga gccggaaacc gcaccactgt ccgcgccacc 601 Asp Asn	7
toggaaccac otocagcaaa ggacacaccg otgtgaccga tacgcacacc ggaccgacac 607	7
cggccgacgc ggtacc 609	3
<210> 16 <211> 401 <212> PRT <213> Streptomyces antibioticus	
<400> 16 Met Glu Asp Ser Glu Leu Gly Arg Arg Leu Gln Met Leu Arg Gly Met 1 5 10 15	
Gln Trp Val Phe Gly Ala Asn Gly Asp Pro Tyr Ala Arg Leu Leu Cys 20 25 30	
Gly Met Glu Asp Asp Pro Ser Pro Phe Tyr Asp Ala Ile Arg Thr Leu 35 40 45	

Gly Glu Leu His Arg Ser Arg Thr Gly Ala Trp Val Thr Ala Asp Pro Gly Leu Gly Gly Arg Ile Leu Ala Asp Arg Lys Ala Arg Cys Pro Glu 70 Gly Ser Trp Pro Val Arg Ala Lys Thr Asp Gly Leu Glu Gln Tyr Val Leu Pro Gly His Gln Ala Phe Leu Arg Leu Glu Arg Glu Glu Ala Glu 105 Arg Leu Arg Glu Val Ala Ala Pro Val Leu Gly Ala Ala Ala Val Asp Ala Trp Arg Pro Leu Ile Asp Glu Val Cys Ala Gly Leu Ala Lys Gly Leu Pro Asp Thr Phe Asp Leu Val Glu Glu Tyr Ala Gly Leu Val Pro Val Glu Val Leu Ala Arg Ile Trp Gly Val Pro Glu Glu Asp Arg Ala Arg Phe Gly Arg Asp Cys Arg Ala Leu Ala Pro Ala Leu Asp Ser Leu 185 Leu Cys Pro Gln Gln Leu Ala Leu Ser Lys Asp Met Ala Ser Ala Leu Glu Asp Leu Arg Leu Leu Phe Asp Gly Leu Asp Ala Thr Pro Arg Leu 215 220 Ala Gly Pro Ala Asp Gly Asp Gly Thr Ala Val Ala Met Leu Thr Val 230 Leu Leu Cys Thr Glu Pro Val Thr Thr Ala Ile Gly Asn Thr Val Leu 250 Gly Leu Leu Pro Gly Gln Trp Pro Val Pro Cys Thr Gly Arg Val Ala Ala Gly Gln Val Ala Gly Gln Ala Leu His Arg Ala Val Ser Tyr Arg Ile Ala Thr Arg Phe Ala Arg Glu Asp Leu Glu Leu Ala Gly Cys Glu Val Lys Ser Gly Asp Glu Val Val Leu Ala Gly Ala Ile Gly Arg Asn Gly Pro Ser Ala Ala Ala Pro Pro Ala Pro Pro Gly Pro Ala Ala

350

330

Pro Pro Ala Pro Ser Val Phe Gly Ala Ala Phe Glu Asn Ala Leu

345

340

Ala Glu Pro Leu Val Arg Ala Val Thr Gly Ala Ala Leu Gln Ala Leu Ala Glu Gly Pro Pro Arg Leu Thr Ala Ala Gly Pro Val Val Arg Arg 375 380 Arg Arg Ser Pro Val Val Gly Gly Leu His Arg Ala Pro Val Ala Ala 390 395 Ala <210> 17 <211> 426 <212> PRT <213> Streptomyces antibioticus <400> 17 Met Met Met Thr Thr Phe Ala Ala Asn Thr His Phe Gln Pro Leu Val Pro Leu Ala Trp Ala Leu Arg Thr Ala Gly His Glu Val Arg Val Val Ser Gln Pro Ser Leu Ser Asp Val Val Thr Gln Ala Gly Leu Thr Ser 40 Val Pro Val Gly Thr Glu Ala Pro Val Glu Gln Phe Ala Ala Thr Trp Gly Asp Asp Ala Tyr Ile Gly Val Asn Ser Ile Asp Phe Thr Gly Asn 70 Asp Pro Gly Leu Trp Thr Trp Pro Tyr Leu Leu Gly Met Glu Thr Met Leu Val Pro Ala Phe Tyr Glu Leu Leu Asn Asn Glu Ser Phe Val Asp 105 Gly Val Val Glu Phe Ala Arg Asp Trp Arg Pro Asp Leu Val Ile Trp 115 Glu Pro Leu Thr Phe Ala Gly Ala Val Ala Ala Arg Val Thr Gly Ala Ala His Ala Arg Leu Pro Trp Gly Gln Glu Ile Thr Leu Arg Gly Arg Gln Ala Phe Leu Ala Glu Arg Ala Leu Gln Pro Phe Glu His Arg Glu 170

Asp Pro Thr Ala Glu Trp Leu Gly Arg Met Leu Asp Arg Tyr Gly Cys

Ser Phe Asp Glu Glu Met Val Thr Gly Gln Trp Thr Ile Asp Thr Leu

200

185

190

205

180

195

Pro Arg Ser Met Arg Leu Glu Leu Ser Glu Glu Leu Arg Thr Leu Asp 210 215 220

Met Arg Tyr Val Pro Tyr Asn Gly Pro Ala Val Val Pro Pro Trp Val 225 230 · 235 240

Trp Glu Pro Cys Glu Arg Pro Arg Val Cys Leu Thr Ile Gly Thr Ser 245 250 255

Gln Arg Asp Ser Gly Arg Asp His Val Pro Leu Asp His Leu Leu Asp 260 265 270

Ser Leu Ala Asp Val Asp Ala Glu Ile Val Ala Thr Leu Asp Thr Thr 275 280 285

Gln Glu Arg Leu Arg Gly Ala Ala Pro Gly Asn Val Arg Leu Val 290 295 300

Asp Phe Val Pro Leu His Ala Leu Met Pro Thr Cys Ser Ala Ile Val 305 310 315 320

His His Gly Gly Pro Gly Thr Trp Ser Thr Ala Ala Leu His Gly Val 325 330 335

Pro Gln Ile Ile Leu Asp Thr Ser Trp Asp Thr Pro Val Arg Ala Gln 340 345 350

Arg Met Gln Gln Leu Gly Ala Gly Leu Ser Met Pro Val Gly Glu Leu 355 . 360 . 365

Gly Val Glu Ala Leu Arg Asp Arg Val Leu Arg Leu Gly Glu Pro 370 375 380

Glu Phe Arg Ala Gly Ala Glu Arg Ile Arg Ala Glu Met Leu Ala Met 385 390 395 400

Pro Ala Pro Gly Asp Val Val Pro Asp Leu Glu Arg Leu Thr Ala Glu 405 410 415

His Ala Thr Gly Ala Met Ala Gly Arg Arg 420 425

<210> 18

<211> 426

<212> PRT

<213> Streptomyces antibioticus

<400> 18

Met Arg Val Leu Leu Thr Cys Phe Ala Asn Asp Thr His Phe His Gly
1 5 10 15

Leu Val Pro Leu Ala Trp Ala Leu Arg Ala Ala Gly His Glu Val Arg
20 25 30

Val Ala Ser Gln Pro Ala Leu Ser Asp Thr Ile Thr Gln Ala Gly Leu

Thr	Ala 50	Val	Pro	Val	Gly	Arg 55	Asp	Thr	Ala	Phe	Leu 60	Glu	Leu	Met	Gly
Glu 65	Ile	Gly	Ala	Asp	Val 70	Gln	Lys	Tyr	Ser	Thr 75	Gly	Ile	Asp	Leu	Gl _y
Val	Arg	Ala	Glu	Leu 85	Thr	Ser	Trp	Glu	Tyr 90	Leu	Leu	Gly	Met	His 95	Thr
Thr	Leu	Val	Pro 100	Thr	Phe	Tyr	Ser	Leu 105	Val	Asn	Asp	Glu	Pro 110	Phe	Val
Asp	Gly	Leu 115	Val	Ala	Leu	Thr	Arg 120	Ala	Trp	Arg	Pro	Asp 125	Leu	Ile	Leu
Trp	Glu 130	His	Phe	Ser	Phe	Ala 135	Gly	Ala	Leu	Ala	Ala 140	Arg	Ala	Thr	GlΣ
Thr 145	Pro	His	Ala	Arg	Val 150	Leu	Trp	Gly	Ser	Asp 155	Leu	Ile	Val	Arg	Phe 160
Arg	Arg	Asp	Phe	Leu 165	Ala	Glu	Arg	Ala	Asn 170	Arg	Pro	Ala	Glu	His 175	Arc
Glu	Asp	Pro	Met 180	Ala	Glu	Trp	Leu	Gly 185	Trp	Ala	Ala	Glu	Arg 190	Leu	Gly
Ser	Thr	Phe 195	Asp	Glu	Glu	Leu	Val 200	Thr	Gly	Gln	Trp	Thr 205	Ile	Asp	Pro
Leu	Pro 210	Arg	Ser	Met	Arg	Leu 215	Pro	Thr	Gly	Thr	Thr 220	Thr	Val	Pro	Met
Arg 225	Tyr	Val	Pro	Tyr	Asn 230	Gly	Arg	Ala	Val	Val 235	Pro	Ala	Trp	Val	Arg 240
Gln	Arg	Ala	Arg	Arg 245	Pro	Arg	Ile	Cys	Leu 250	Thr	Leu	Gly	Val	Ser 255	Ala
Arg	Gln	Thr	Leu 260	Gly	Asp	Gly	Val	Ser 265	Leu	Ala	Glu	Val	Leu 270	Ala	Ala
Leu	Gly	Asp 275	Val	Asp	Ala	Glu	Ile 280	Val	Ala	Thr	Leu	Asp 285	Ala	Ser	Glr
Arg	Lys 290	Leu	Leu	Gly	Pro	Val 295.		Asp	Asn	Val	Arg 300	Leu	Val	Asp	Phe
Val 305	Pro	Leu	His	Ala	Leu 310	Met	Pro	Thr	Cys	Ser 315	Ala	Ile	Val	His	His 320
Gly	Gly	Ala	Gly	Thr 325	Trp	Leu	Thr	Ala	Ala 330	Val	His	Glỳ	Val	Pro 335	Glr

Ile Val Leu Gly Asp Leu Trp Asp Asn Leu Leu Arg Ala Arg Gln Thr

340 345 350

Gln Ala Ala Gly Ala Gly Leu Phe Ile His Pro Ser Glu Val Thr Ala 355 360 365

Ala Gly Leu Gly Glu Gly Val Arg Arg Val Leu Thr Asp Pro Ser Ile 370 375 380

Arg Ala Ala Ala Gln Arg Val Arg Asp Glu Met Asn Ala Glu Pro Thr 385 390 395 400

Pro Gly Glu Val Val Thr Val Leu Glu Arg Leu Ala Ala Ser Gly Gly 405 410 415

Arg Gly Arg Gly Gly Asn His Ala Gly 420 425

<210> 19

<211> 386

<212> PRT

<213> Streptomyces antibioticus

<400> 19

Met Ser Tyr Asp Asp His Ala Val Leu Glu Ala Ile Leu Arg Cys Ala 1 5 10 15

Gly Gly Asp Glu Arg Phe Leu Leu Asn Thr Val Glu Glu Trp Gly Ala 20 25 30

Ala Glu Ile Thr Ala Ala Leu Val Asp Glu Leu Leu Phe Arg Cys Glu 35 40 45

Ile Pro Gln Val Gly Gly Glu Ala Phe Ile Gly Leu Asp Val Leu His 50 55 60

Gly Ala Asp Arg Ile Ser His Val Leu Gln Val Thr Asp Gly Lys Pro 65 70 75 80

Val Thr Ser Ala Glu Pro Ala Gly Gln Glu Leu Gly Gly Arg Thr Trp 85 90 95

Ser Ser Arg Ser Ala Thr Leu Leu Arg Glu Leu Phe Gly Pro Pro Ser

Gly Arg Thr Ala Gly Gly Phe Gly Val Ser Phe Leu Pro Asp Leu Arg 115 120 125

Gly Pro Arg Thr Met Glu Gly Ala Ala Leu Ala Ala Arg Ala Thr Asn 130 135 140

Val Val Leu His Ala Thr Thr Asn Glu Thr Pro Pro Leu Asp Arg Leu 145 150 155 160

Ala Leu Arg Tyr Glu Ser Asp Lys Trp Gly Gly Val His Trp Phe Thr 165 170 175 Gly His Tyr Asp Arg His Leu Arg Ala Val Arg Asp Gln Ala Val Arg Ile Leu Glu Ile Gly Ile Gly Gly Tyr Asp Asp Leu Leu Pro Ser Gly 200 Ala Ser Leu Lys Met Trp Lys Arg Tyr Phe Pro Arg Gly Leu Val Phe 215 Gly Val Asp Ile Phe Asp Ser Arg Ala Thr Ser Arg Val Ser Arg 230 235 Arg Ser Ala Ala Arg Gln Asp Asp Pro Glu Phe Met Arg Arg Val Ala 245 250 Glu Glu His Gly Pro Phe Asp Val Ile Ile Asp Asp Gly Ser His Ile Asn Ala His Met Arg Thr Ser Phe Ser Val Met Phe Pro His Leu Arg Asn Gly Gly Phe Tyr Val Ile Glu Asp Thr Phe Thr Ser Tyr Trp Pro 295 Gly Tyr Gly Gly Pro Ser Gly Ala Arg Cys Pro Ser Gly Thr Thr Ala Leu Glu Met Val Lys Gly Leu Ile Asp Ser Val His Tyr Glu Glu Arg 330 Pro Asp Gly Ala Ala Thr Ala Asp Tyr Ile Ala Arg Asn Leu Val Gly Leu His Ala Tyr Gln Thr Thr Ser Ser Ser Arg Arg Ala Ile Asn 360 Lys Glu Gly Gly Ile Pro His Thr Val Pro Arg Glu Pro Phe Trp Asn 375 Asp Asn 385 <210> 20 <211> 738 <212> DNA <213> Streptomyces antibioticus <220> <221> CDS <222> (1)..(738) <223> /gene= "oleM" /note= "SEQ ID No. 15 from 3992 to 4729" <220> <221> mat_peptide <222> (1)

)> 20															
		_	_	_		_			999 Gly 10							48
									cgg Arg							96
		_	_			_		_	cgc Arg	-			_	-		144
			_	-		_	_		acg Thr		_					192
									ggt Gly							240
_	_	_		_	_		_	_	ccg Pro 90			-	_			288
	_	_	_			_	_		cca Pro	_	_			_		336
_	_		_		_			_	gcc Ala			-	_		_	384
									acc Thr							432
									acc Thr							480
									cgg Arg 170							528
									cgc Arg							576
									cac His							624
									acg Thr							672

ggc tac acc o Gly Tyr Thr V 225					
ttc gtc ggc a					738
<210> 21 <211> 246 <212> PRT <213> Strepto	omyces anti	bioticus			
<400> 21 Met Arg Ala A 1	Asp Thr Glu 5	Pro Thr Th	r Gly Tyr 10	Glu Asp Glu	Phe Ala 15
Glu Ile Tyr A	Asp Ala Val 20	Tyr Arg Gl		Lys Asp Tyr 30	-
Glu Ala Lys A	Asp Val Ala	Asp Leu Va 40	l Arg Asp	Arg Val Pro 45	Asp Ala
Ser Ser Leu I 50	Leu Asp Val	Ala Cys Gl 55	y Thr Gly	Ala His Leu 60	Arg His
Phe Ala Thr I 65	Leu Phe Asp 70	Asp Ala Ar	g Gly Leu 75	Glu Leu Ser	Ala Ser 80
Met Leu Asp 1	Ile Ala Arg 85	Ser Arg Me	t Pro Gly 90	Val Pro Leu	His Gln 95
Gly Asp Met A	Arg Ser Phe 100	Asp Leu Gl		Val Ser Ala 110	
Cys Met Phe S	Ser Ser Val	Gly His Le 120	u Ala Thr	Thr Ala Glu 125	Leu Asp
Ala Thr Leu A	Arg Cys Phe	Ala Arg Hi 135		Pro Gly Gly 140	Val Ala
Val Ile Glu I 145	Pro Trp Trp 150	Phe Pro Gl	u Thr Phe 155	Thr Asp Gly	Tyr Val 160
Ala Gly Asp 1	Ile Val Arg 165	Val Asp Gl	y Arg Thr 170	Ile Ser Arg	Val Ser 175
His Ser Val A	Arg Asp Gly 180	Gly Ala Th	_	Glu Ile His 190	-
Ile Ala Asp A	Ala Glu His	Gly Pro Ar 200	g His Leu	Val Glu His 205	His Arg
Ile Thr Leu E 210	Phe Pro Arg	His Ala Ty 215		Ala Tyr Glu 220	Lys Ala

```
Gly Tyr Thr Val Glu Tyr Leu Asp Gly Gly Pro Ser Gly Arg Gly Leu
225
                                                              240
Phe Val Gly Thr Arg Thr
                245
<210> 22
<211> 19
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 22
tcctcgatgg agacctgcc
                                                                    19
<210> 23
<211> 19
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 23
gagaccatgc ccagggagt
                                                                    19
<210> 24
<211> 19
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 24
tctgggagcc gctcacctt
                                                                    19
<210> 25
<211> 19
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 25
                                                                    19
gacgaggccg aagaggtgg
<210> 26
```

- 49 -

```
<211> 19
<212> DNA
<213> Artificial sequence
<220>
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 26
gcacaccgga atggatgcg
                                                                    19
<210> 27
<211> 19
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 27
ccgtcgagct ctgaggtaa
                                                                    19
<210> 28
<211> 19
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 28
gcccgagccg cacgtgcgt
                                                                    19
<210> 29
<211> 20
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 29
tgcacgcgct gctgccgacc
                                                                    20
<210> 30
<211> 20
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 30
ttggcgaagt cgaccaggtc
                                                                    20
```

```
<210> 31
<211> 23
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 31
gccgctcggc acggtgaact tca
                                                                    23
<210> 32
<211> 24
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 32
atgcgcgtcg tcttctcctc catg
                                                                    24
<210> 33
<211> 21
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 33
tcatcgtggt tctctccttc c
                                                                    21
<210> 34
<211> 23
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 34
ggaattcatg accacgaccg atc
                                                                    23
<210> 35
<211> 28
<212> DNA
<213> Artificial sequence
<220>
<223> Description of Artificial Sequence: synthetic oligonucleotide
```

- 51 -

```
<400> 35
cgctccaggt gcaatgccgg gtgcaggc
                                                                    28
<210> 36
<211> 22
<212> DNA
<213> Artificial sequence
<220>
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 36
gatcacgctc ttcgagcggc ag
                                                                    22
<210> 37
<211> 21
<212> DNA
<213> Artificial sequence
<220>
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 37
gaactcggtg gagtcgatgt c
                                                                    21
<210> 38
<211> 21
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 38
gttgtcgatc aagacccgca c
                                                                    21
<210> 39
<211> 22
<212> DNA
<213> Artificial sequence
<220>
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 39
catcgtcaag gagttcgacg gt
                                                                    22
<210> 40
<211> 25
<212> DNA
<213> Artificial sequence
```

```
<223> Description of Artificial Sequence: synthetic oligonucleotide
 <400> 40
 tgcgcaggtc catgttcacc acgtt
                                                                    25
 <210> 41
 <211> 20
 <212> DNA
 <213> Artificial sequence
 <223> Description of Artificial Sequence: synthetic oligonucleotide
 <400> 41
 gctacgccct ggagagcctg
                                                                    20
 <210> 42
 <211> 21
 <212> DNA
 <213> Artificial sequence
 <223> Description of Artificial Sequence: synthetic oligonucleotide
 <400> 42
 gtcgcggtcg gagagcacga c
                                                                    21
 <210> 43
 <211> 21
 <212> DNA
<213> Artificial sequence
 <223> Description of Artificial Sequence: synthetic oligonucleotide
 <400> 43
 gccagctcgg cgacgtccat c
                                                                    21
 <210> 44
 <211> 19
 <212> DNA
 <213> Artificial sequence
 <223> Description of Artificial Sequence: synthetic oligonucleotide
 <400> 44
 cgacgaggtc gtgcatcag
                                                                     19
 <210> 45
```

```
<211> 56
<212> DNA
<213> Artificial sequence
<220>
<223> Description of Artificial Sequence: synthetic oligonucleotide
aattgatcaa ggtgaacacg gtcatgcgca ggatcctcga gcggaactcc atgggg
                                                                   56
<210> 46
<211> 56
<212> DNA
<213> Artificial sequence
<220>
<223> Description of Artificial Sequence: synthetic oligonucleotide
ccccatggag ttccgctcga ggatcctgcg catgaccgtg ttcaccttga tcaatt
                                                                   56
<210> 47
<211> 32
<212> DNA
<213> Artificial sequence
<220>
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 47
aactcggtgg agtcgatgtc gtcgctgcgg aa
                                                                   32
<210> 48
<211> 27
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 48
caatatagga aggatcaaga ggttgac
                                                                   27
<210> 49
<211> 39
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<220>
```

- 54 -

<pre><210> 50 <211> 33 <212> DNA <213> Artificial sequence </pre> <pre><220> <223> Description of Artificial Sequence: synthetic oligonucleotide <400> 50 aggagcacta gtgcgggtac tgctgacgtc ctt</pre>	<400> 49 tccggaggtg tgctgtcgga cggacttgtc ggtcggaaa	39
<pre><223> Description of Artificial Sequence: synthetic oligonucleotide <400> 50 aggagcacta gtgcgggtac tgctgacgtc ctt</pre>	<211> 33	
aggagcacta gtgcgggtac tgctgacgtc ctt 33 <210> 51 <211> 37 <212> DNA <213> Artificial sequence <220> <223> Description of Artificial Sequence: synthetic oligonucleotide <440> 51 gggggatccc atatgcgggt actgctgacg tccttcg 37 <210> 52 <211> 37 <212> DNA <213> Artificial sequence <220> <221> Siggggatccc atatgcgggt actgctgacg tccttcg 37 <212> DNA <213> Artificial sequence <220> <223> Description of Artificial Sequence: synthetic oligonucleotide <4400> 52 gaaaagatct gccggcgtgg cggcggtga gttcctc 37 <210> 53 <211> 27 <212> DNA <213> Artificial sequence <220> <223> Description of Artificial Sequence: synthetic oligonucleotide <440> 53 <211> 27 <212> DNA <213> Artificial sequence <220> <223> Description of Artificial Sequence: synthetic oligonucleotide <4400> 53 agcggcttga tcgtgttgga ccagtac 27 <210> 54 <211> 27 <211> DNA <211> 27 <212> DNA		oligonucleotide
<pre><211> 37 <212> DNA <213> Artificial sequence </pre> <pre><220> <223> Description of Artificial Sequence: synthetic oligonucleotide <400> 51 gggggatccc atatgcgggt actgctgacg tccttcg</pre>		. 33
<pre><223> Description of Artificial Sequence: synthetic oligonucleotide <400> 51 gggggatccc atatgcgggt actgctgacg tccttcg</pre>	<211> 37 <212> DNA	
gggggatccc atatgcgggt actgctgacg tccttcg 37 <210 > 52 <211 > 37 <212 > DNA <213 > Artificial sequence <220 > <223 > Description of Artificial Sequence: synthetic oligonucleotide <400 > 52 gaaaagatct gccggcgtgg cggcgcgtga gttcctc 37 <210 > 53 <211 > 27 <212 > DNA <213 > Artificial sequence <220 > <222 > <223 > Description of Artificial Sequence: synthetic oligonucleotide <400 > 53 <211 > 27 <212 > DNA <213 > Artificial sequence <220 > <223 > Description of Artificial Sequence: synthetic oligonucleotide <400 > 53 agcggcttga tcgtgttgga ccagtac 27 <210 > 54 <211 > 27 <212 > DNA		oligonucleotide
<pre><211> 37 <212> DNA <213> Artificial sequence </pre> <pre><220> <223> Description of Artificial Sequence: synthetic oligonucleotide <400> 52 gaaaagatct gccggcgtgg cggcgcgtga gttcctc 37 </pre> <pre><210> 53 <211> 27 <212> DNA <213> Artificial sequence </pre> <pre><220> <223> Description of Artificial Sequence: synthetic oligonucleotide <400> 53 agcggcttga tcgtgttgga ccagtac 27 </pre> <pre><210> 54 <211> 27 <212> DNA</pre>		37
<pre><223> Description of Artificial Sequence: synthetic oligonucleotide <400> 52 gaaaagatct gccggcgtgg cggcgcgtga gttcctc 37 <210> 53 <211> 27 <212> DNA <213> Artificial sequence <220> <223> Description of Artificial Sequence: synthetic oligonucleotide <400> 53 agcggcttga tcgtgttgga ccagtac 27 <210> 54 <211> 27 <212> DNA</pre>	<211> 37 <212> DNA	
<pre>gaaaagatct gccggcgtgg cggcgcgtga gttcctc <210> 53 <211> 27 <212> DNA <213> Artificial sequence <220> <223> Description of Artificial Sequence: synthetic oligonucleotide <400> 53 agcggcttga tcgtgttgga ccagtac 27 <210> 54 <211> 27 <212> DNA</pre>		oligonucleotide
<211> 27 <212> DNA <213> Artificial sequence <220> <223> Description of Artificial Sequence: synthetic oligonucleotide <400> 53 agcggcttga tcgtgttgga ccagtac 27 <210> 54 <211> 27 <212> DNA		37
<223> Description of Artificial Sequence: synthetic oligonucleotide <400> 53 agcggcttga tcgtgttgga ccagtac 27 <210> 54 <211> 27 <212> DNA	<211> 27 <212> DNA	
agcggcttga tcgtgttgga ccagtac 27 <210> 54 <211> 27 <212> DNA		oligonucleotide
<211> 27 <212> DNA		27
	<211> 27 <212> DNA	

- 55 **-**

<220> <223>	Description of Artificial Sequence	e: synthetic	oligonucleotide
<400> ggccta	54 atgtg gactacgtgt tgaacgt		27
<210><211><211><212><213>	31 .		
<220> <223>	Description of Artificial Sequence	e: synthetic	oligonucleotide
<400> aacgc	55 ctcgt cctgcagcgg agacacgaac a		31
<210><211><211><212><213>	27		
<220> <223>	Description of Artificial Sequence	e: synthetic	oligonucleotide
<400> ttcgc	56 tecce gatgaacaca actegta		27
<220>	35 DNA Artificial sequence	e: synthetic	oligonucleotide
<400>			35
<210><211><211><212><213>	32		
<220> <223>	Description of Artificial Sequence	e: synthetic	oligonucleotide
<400> cggga	58 teete ategtggtte teteetteet ge		32
<210> <211>			

- 56 -

```
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 59
cgggtaccat gcgcgtcgtc ttctcctcca tg
                                                                    32
<210> 60
<211> 29
<212> DNA
<213> Artificial sequence
<223> Description of Artificial Sequence: synthetic oligonucleotide
<400> 60
cgggtacctc atcgtggttc tctccttcc
                                                                    29
<210> 61
<211> 13
<212> PRT
<213> Artificial sequence
<223> Description of Artificial Sequence: peptide
<400> 61
Val Thr Gly Ala Gly Asp Gly Asp Ala Asp Val Gln Ala
```

B's